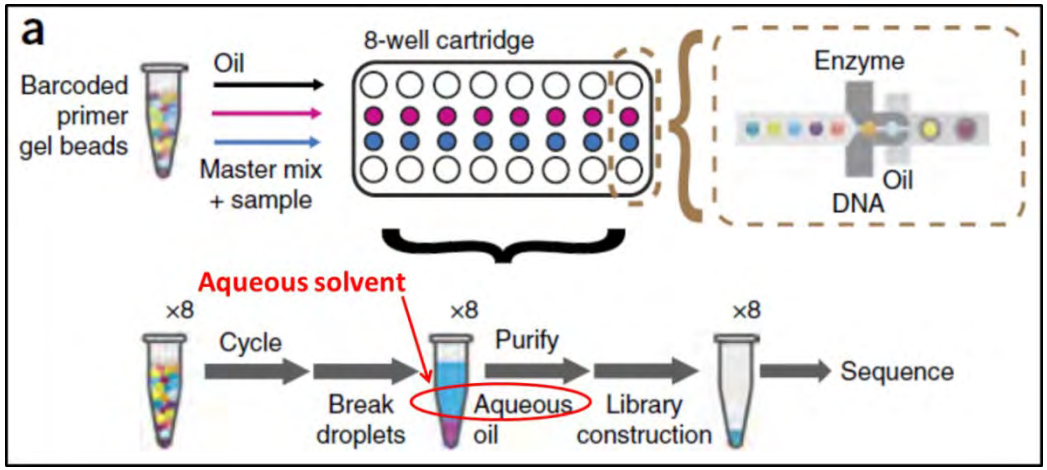
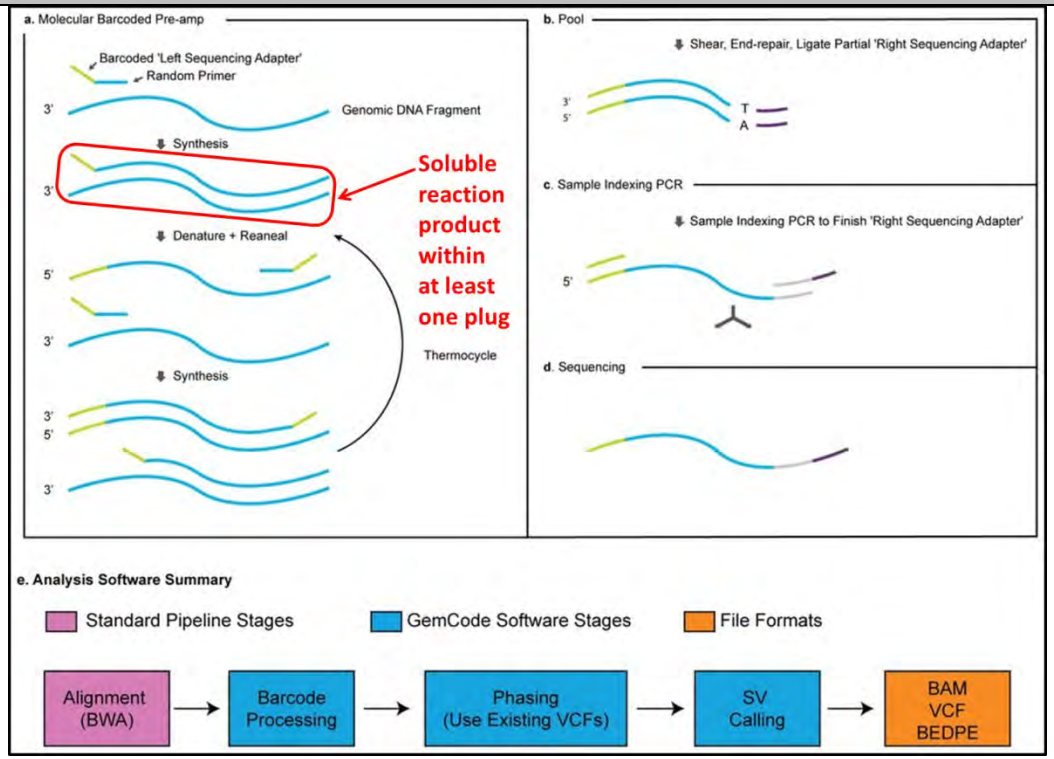
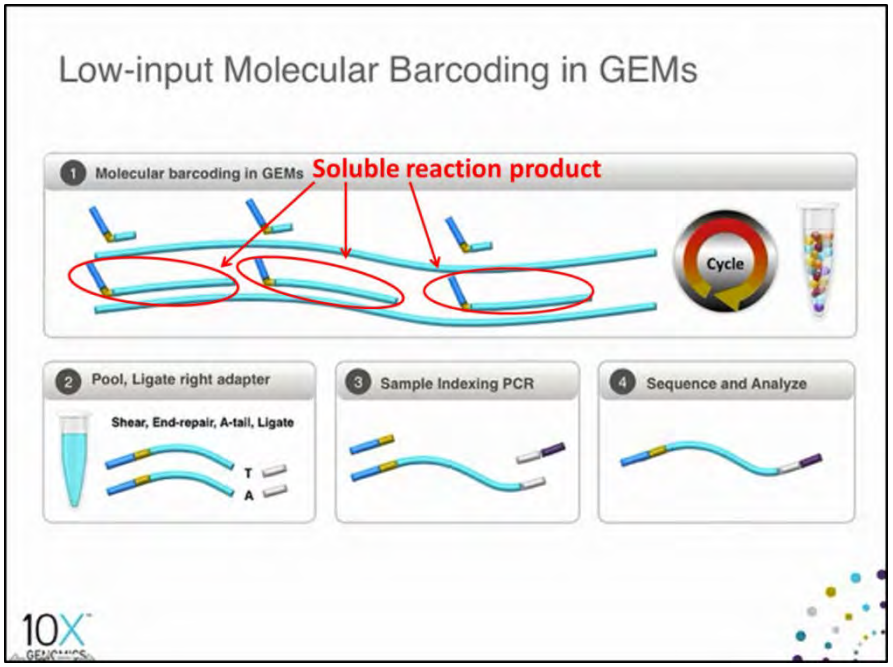
	’091 Claim Language	Infringement Support
		channels. As a result, the plugs contain a solvent (water).  Ex. 5 [*Nature Biotechnology*] at Fig. 1a.
091-11	11. The method of claim 1, wherein the reaction of the plug-fluids forms a soluble reaction product within at least one plug.	**10X’s GemCode platform forms a DNA amplification product, which is soluble within the aqueous plug fluid.** • The DNA amplification process which occurs in the microfluidic droplets of 10X’s GemCode platform is depicted in the figure below in the panel labeled “a. Molecular Barcoded Pre-amp.” This figure is taken from 10X’s recent article in *Nature Biotechnology*, which presents data based on the use of 10X’s GemCode platform. The figure below shows a single stranded “Genomic DNA Fragment” that is extended through the use of a “Random Primer.” The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process.

	’091 Claim Language	Infringement Support

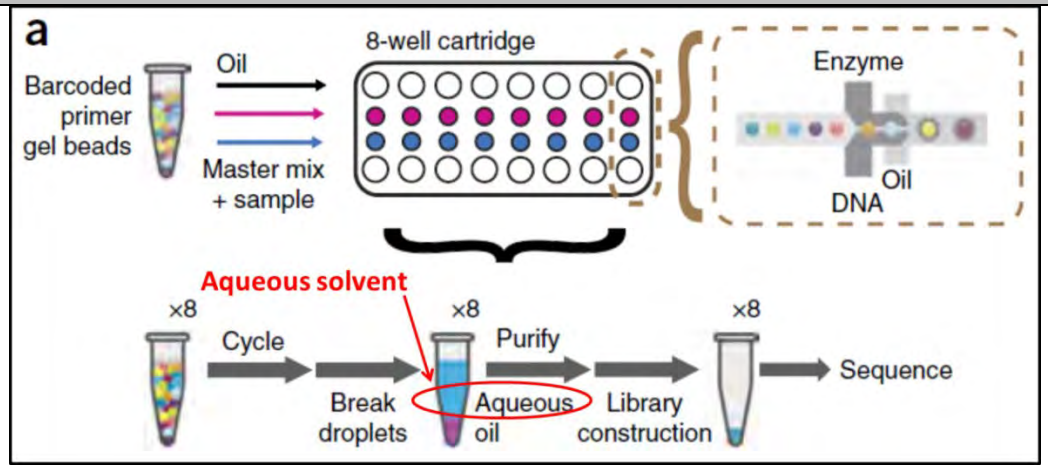


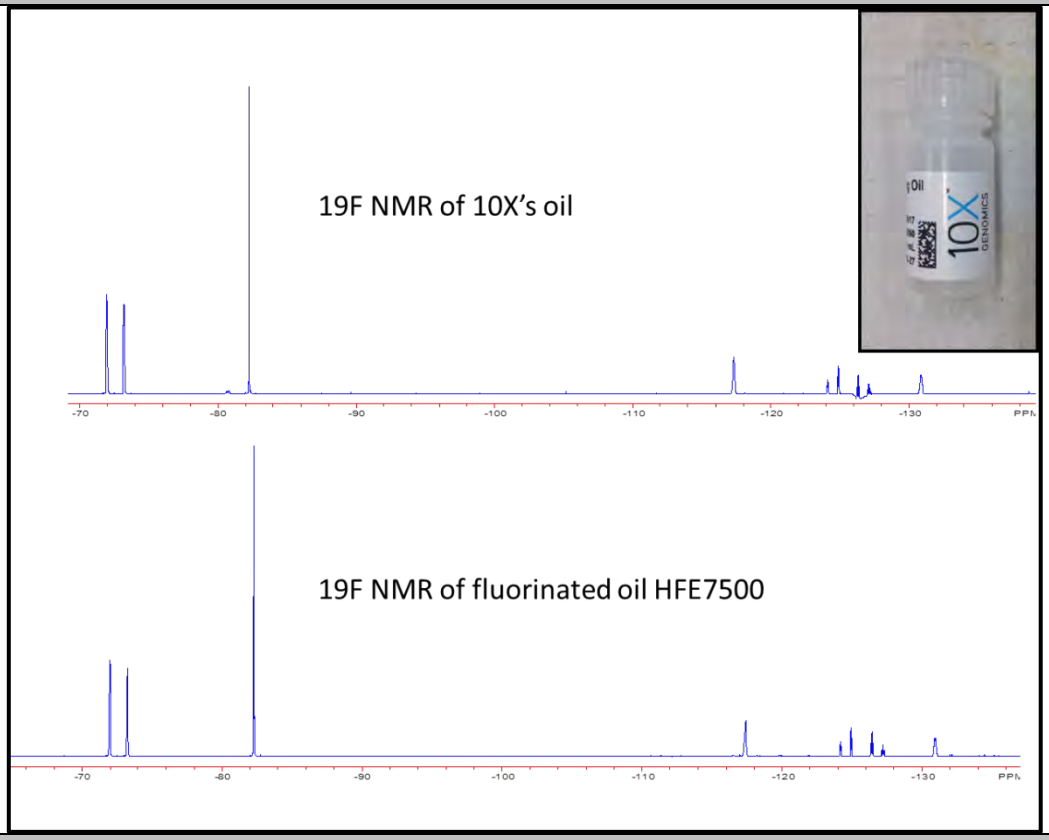
Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X’s publication states, “1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes.” *Id.* at 3432. The DNA amplification product is soluble in water.

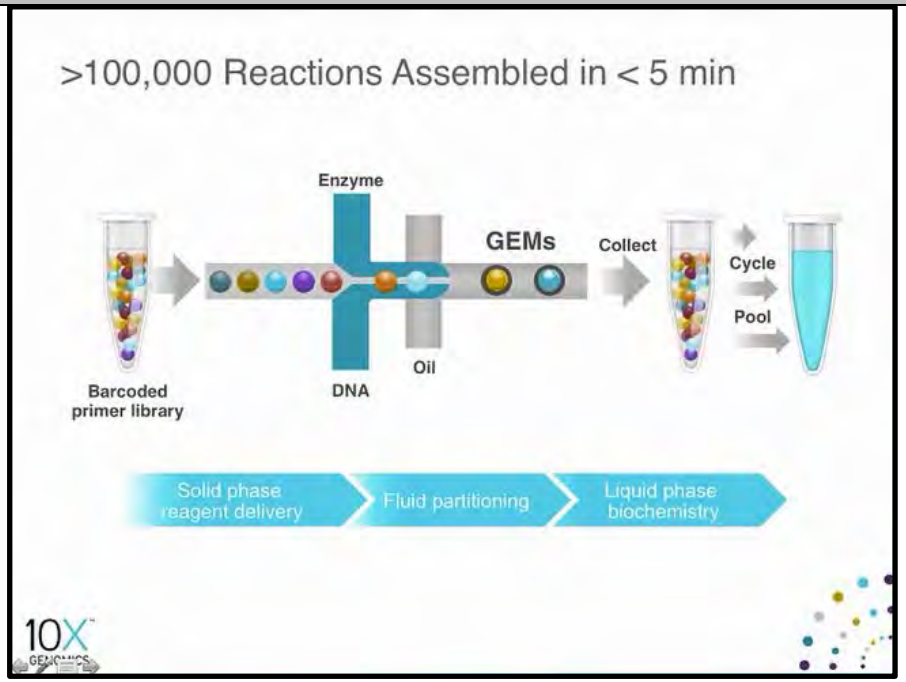
- During his August 2015 webinar, Dr. Schnall-Levin described the DNA amplification reaction that takes place in the droplets with reference to the figure below. “So now the biochemistry that’s happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you’ve broken the droplets and put everything back together in bulk. First you can

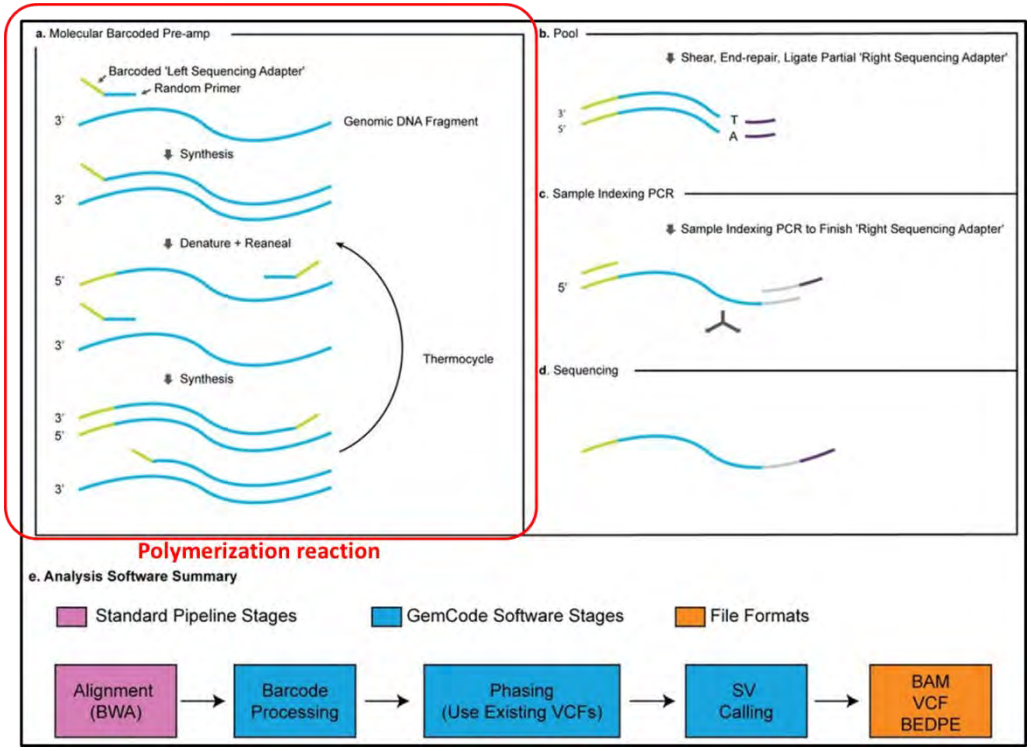
	'091 Claim Language	Infringement Support
		concentrate on the top panel showing the biochemistry that's happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying.*** The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template." Ex. 5 [10X Webinar] at 13:00-53.  • The amplified DNA product is soluble in the aqueous droplets.

	'091 Claim Language	**Infringement Support**
091-23	23. The method of claim 1, further comprising detecting the product of the reaction.	**The product of the DNA amplification reaction is detected by DNA sequencing.** • The DNA that results from the amplification reaction in 10X's product includes additional specialized DNA sequences so that the amplified DNA can be sequenced, and hence detected, on an Illumina DNA sequencing instrument. As 10X explained in its recent *Nature Biotechnology* paper, "[t]o create barcoded DNA molecules for sequencing, we perform an optimized droplet-based assay that introduces a barcode-containing sequencing adapter into new fragments (Online Methods). HMW DNA templates, ranging from ten to several hundred kilobases in size, are randomly distributed in picoliter reaction volumes across >100,000 droplets. Within an individual droplet, gel bead dissolution releases the amplification primer into the partitioned solution. The primer contains the following components: (i) an Illumina P5 flow cell primer sequence, (ii) a 14-bp barcode, (iii) an Illumina R1 sequence (read 1 sequencing primer) and (iv) a 10-bp random primer sequence (Supplementary Fig. 1)." Ex. 5 [Nature Biotechnology] at 2.
091-27	27. The method of claim 1, wherein refractive indices of the carrier-fluid and the plug-fluids are substantially similar.	10X's GemCode platform performs "the method of claim 1, wherein refractive indices of the carrier-fluid and the plug-fluids are substantially similar." • The plug fluid is aqueous. • The carrier fluid is a fluorinated oil comprised primarily of HFE7500. • Water and fluorinated oil have substantially similar refractive indices. **10X's GemCode platform uses aqueous plug fluids.** • The droplets that are formed in 10X's microfluidic device are broken after a DNA amplification reaction is carried out inside the droplet. The fluid that is inside the droplets separates from the oil that originally surrounded and carried the droplets. As depicted below, the interior of the droplet is "Aqueous" and is shown in blue. Thus, the channels that provided the fluids for the interior of the droplets are aqueous fluid channels.

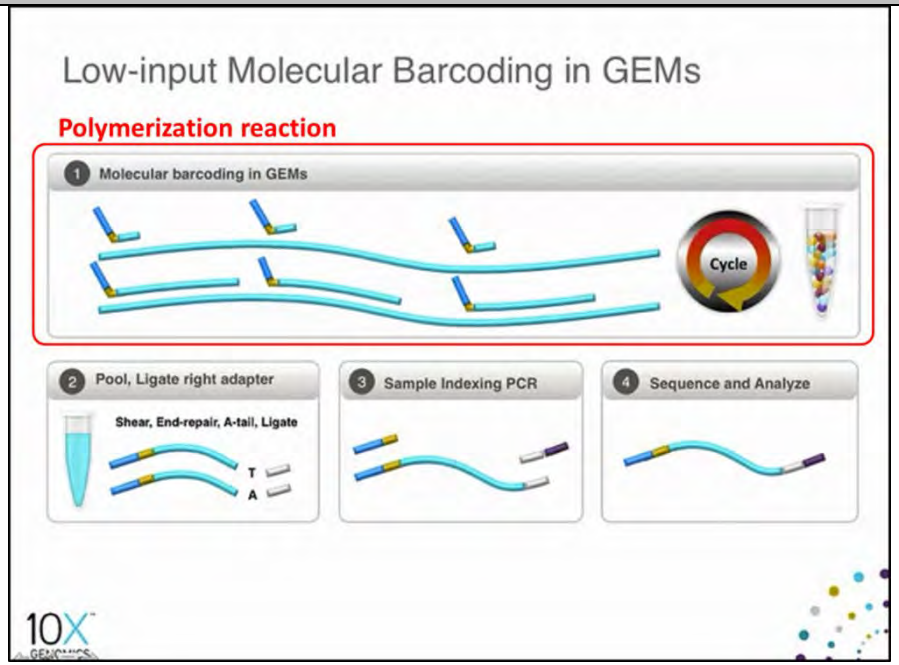
	’091 Claim Language	Infringement Support
		 Ex. 5 [*Nature Biotechnology*] at Fig. 1a. **<u>10X’s GemCode platform uses a fluorinated oil carrier fluid with a refractive index substantially similar to water.</u>** • A comparison of the 19F nuclear magnetic resonance spectrum for 10X’s partitioning oil (i.e., carrier fluid) to the spectrum for the commercially available fluorinated oil HFE7500 reveals that 10X’s partitioning oil consists primarily of HFE7500. HFE7500 has a refractive index of 1.29 and water has a refractive index of 1.333. The refractive index of the carrier fluid and plug fluid are thus substantially similar.

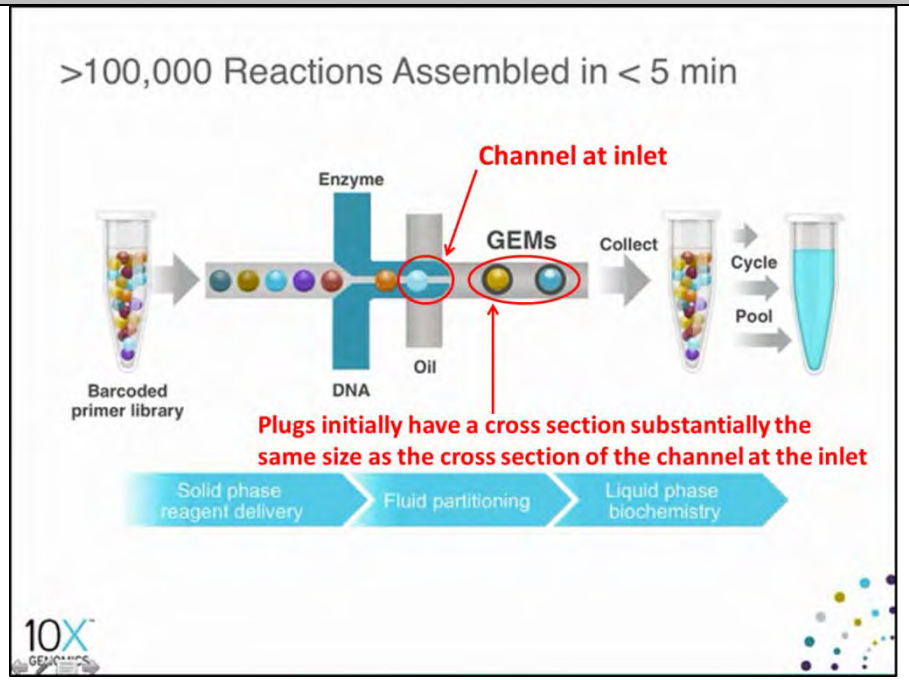
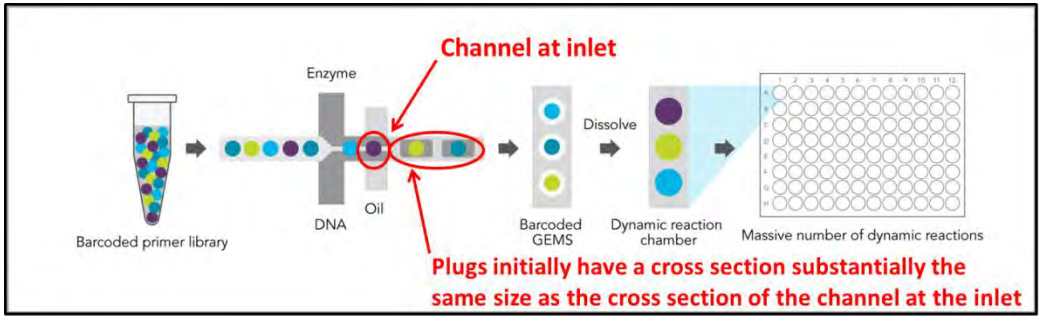
	'091 Claim Language	**Infringement Support**
		
091-29	29. The method of claim 1, further comprising employing a number of devices in parallel.	**<u>10X's GemCode platform uses microfluidic chips with eight channels in parallel allowing for eight samples to be tested in parallel.</u>** • As Dr. Schnall Levin explained during his August 2015 webinar, below is a "cross-section of one of the channels present in [10X's] microfluidic chip. ***If you look at one of our microfluidic chips there would be eight of these channels in parallel such that you can run eight samples at a time."*** Ex. 4 [10X Webinar] at 9:32-47.

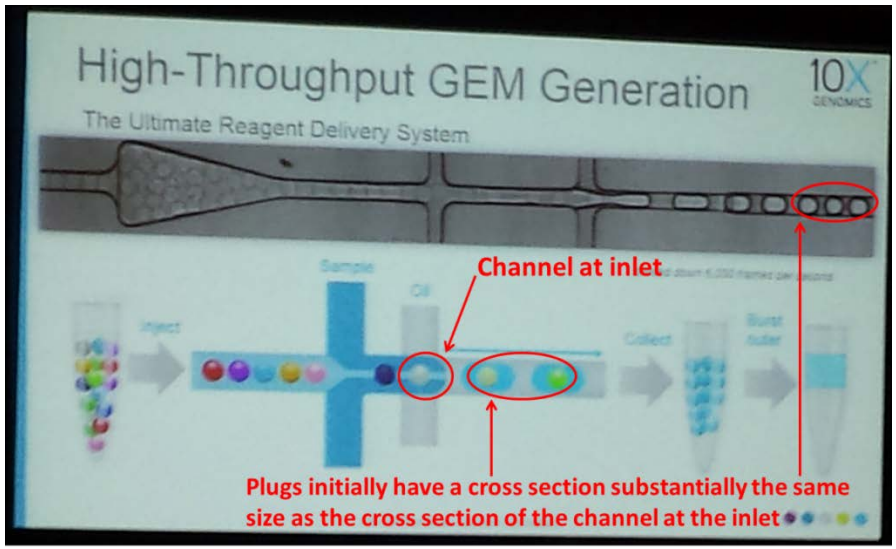
	'091 Claim Language	**Infringement Support**
		
091-31	31. The method of claim 1, wherein the reaction is a polymerization reaction.	**10X's GemCode platform conducts a polymerization reaction in droplets so that it can amplify DNA.** • Polymerase chain reaction ("PCR") involves the use of an extension enzyme, DNA primers, and nucleotides to amplify DNA. The process takes place through a cycling protocol in which DNA is denatured into single strands, and then replicated by an enzyme in a polymerization reaction. The DNA product of this reaction cycle is then used as the starting material for the next round of amplification.

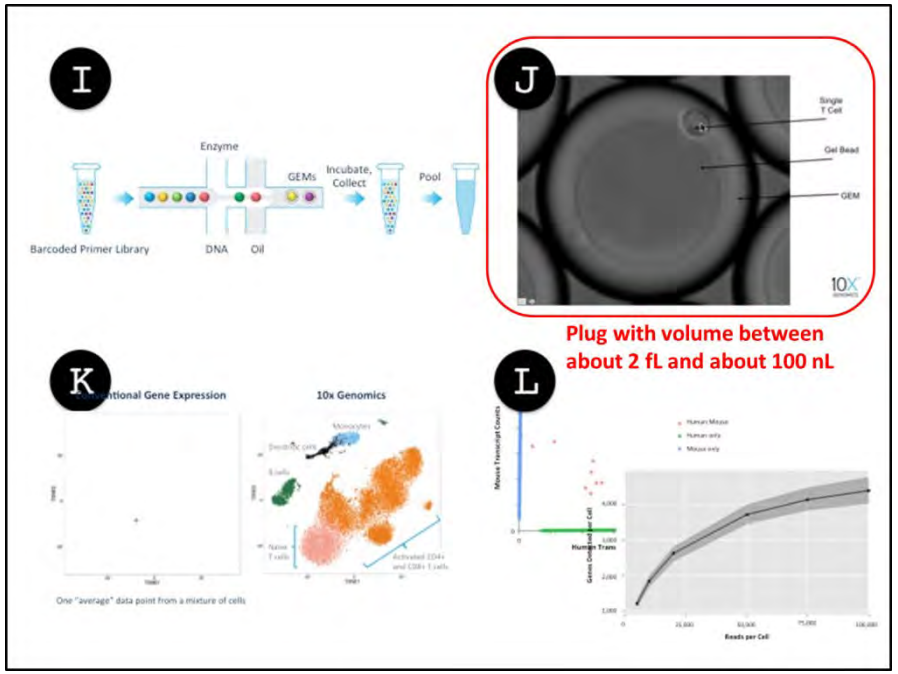
	’091 Claim Language	Infringement Support
		• This process is depicted in the figure below in the panel labeled “a. Molecular Barcoded Pre-amp.” This figure is taken from 10X’s recent article in *Nature Biotechnology*, which presents data based on the use of 10X’s GemCode platform. The figure below shows a single stranded “Genomic DNA Fragment” that is extended through the use of a “Random Primer.” The extension that takes place is a polymerization reaction. The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process.  Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X’s publication states, “1 ng of

	'091 Claim Language	**Infringement Support**
		sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes." *Id.* at 3432. • During his August 2015 webinar, Dr. Schnall-Levin described the DNA amplification reaction, which includes a polymerization reaction, that takes place in the droplets with reference to the figure below. "So now the biochemistry that's happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you've broken the droplets and put everything back together in bulk. First you can concentrate on the top panel showing the biochemistry that's happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying.*** The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template." Ex. 4 [10X Webinar] at 13:00-53.

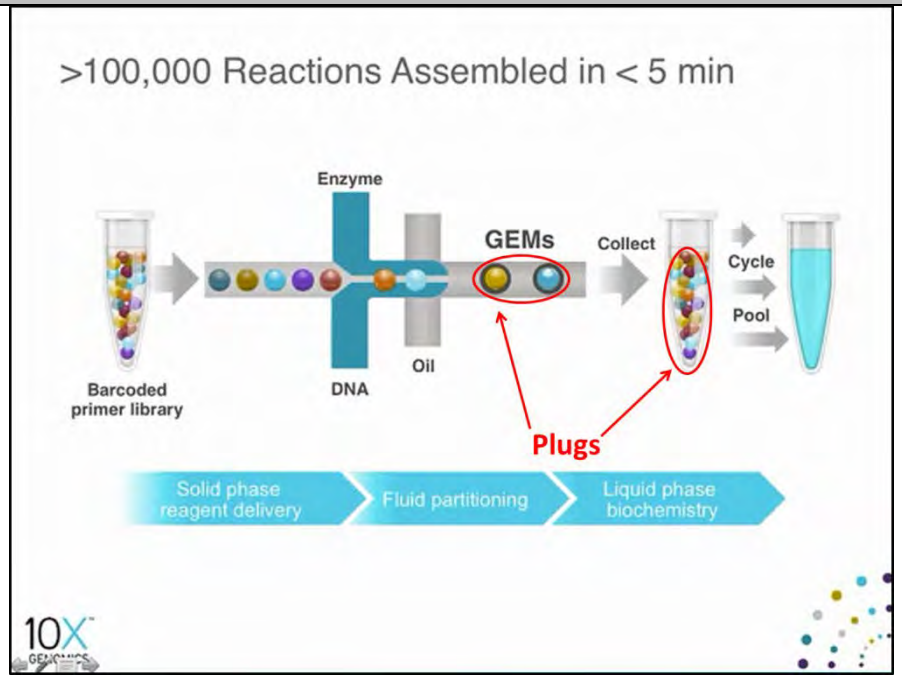
	'091 Claim Language	**Infringement Support**
		
091-33	33. The method of claim 1, wherein each plug initially has a cross section that is substantially the same size as the cross section of the channel at the inlet.	**<u>The microfluidic droplets in 10X's GemCode platform initially have a cross section that is substantially the same size as the cross section of the channel containing the aqueous fluids.</u>** • During his August webinar, Dr. Schnall-Levin explained that the picture below is "a cross-section of one of the ***channel in our microfluidic chip***." *Id.* at 9:33-39. In that picture, each plug labeled GEMs has a cross section substantially the same size as the cross section as the cross section of the center channel.

	’091 Claim Language	Infringement Support
		 • 10x’s website is also consistent in showing that the cross section of the plug is initially substantially the same size as the cross section of the center channel. 

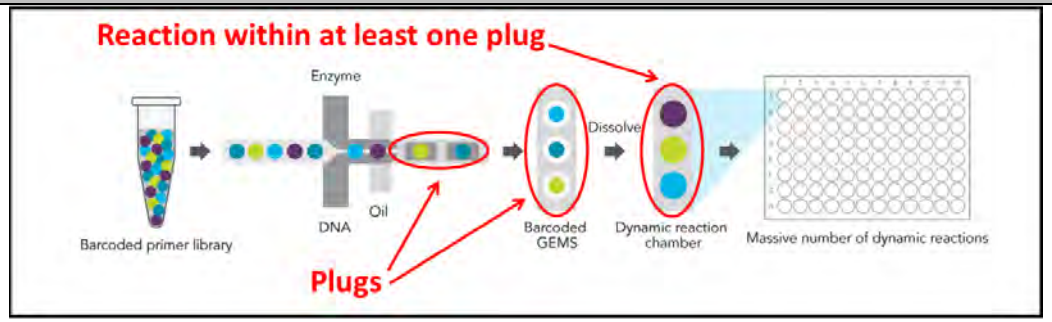
	'091 Claim Language	**Infringement Support**
		• 10x Technologies' 2015 presentation at the JP Morgan healthcare conference further shows a microfluidic system for conducting reactions in plugs, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are the light gray circles and initially have a cross section that is substantially the same as the cross section of the center channel.  Ex. 37 [JP Morgan presentation] at 2.
091-35	35. The method of claim 1, wherein the volume of at least one plug is about 1 femtoliter to about 250 nL.	**10X's droplets have a volume between 1 femtoliters and about 250 nanoliters**. • At the 2016 AGBT conference, 10X provided a workshop in which it described its technology. The figure below from 10X's workshop presentation depicts in Panel J a droplet alongside a "Singe T Cell." Based on the fact that a T cell is roughly 10 µm in

	'091 Claim Language	Infringement Support
		diameter, 10X's droplets are roughly 100 µm in diameter. This leads to a droplet volume in 10X's GemCode platform of roughly 0.5 nanoliters, which is between two femtoliters and one hundred nanoliters.  Ex. 40 [Core Genomics Summary] at __.
091-36a	36. A method of conducting a reaction within at least one plug comprising the steps of:	10X's GemCode platform uses "method of conducting a reaction within at least one plug." • The plugs are microfluidic droplets that are formed in 10X's GemCode platform. • A reaction that is conducted in the plug is a DNA amplification reaction. **10X's GemCode platform is a microfluidic system using "plugs," which 10X refers to as**

	'091 Claim Language	**Infringement Support**
		droplets or "GEMs" • The '091 patent's description of "plugs" includes the following: "'Plugs' in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible." Ex. 11 ['091 patent] at 9:20-23. • On August 5, 2015, Michael Schnall-Levin, 10X's Vice President of Computational Biology and Applications, presented a webinar "about the GemCode platform." Ex. 4 [10X Webinar] at 3:17-3:23; *see also id.* at 3:35-38 ("I'm really excited today to take you through our Platform."). During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms plugs in the manner described by the '091 patent with reference to the below figure: "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." *Id.* at 9:48-10:39.

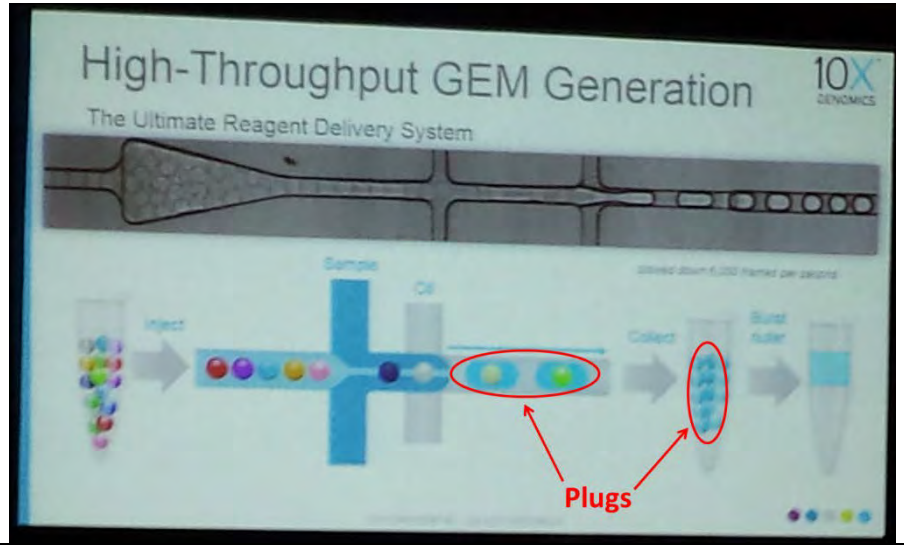
	’091 Claim Language	Infringement Support
		 • 10x’s website is consistent with Dr. Schnall-Levin’s description of 10X’s Platform. 10X’s website states that “[t]he instrument features precise ***microfluidics*** coupled with single button, user-friendly operation.” Ex. 39 [10X Website Excerpts] at 1. The website further states that the 10X chip kit “[c]ontains the ***microfluidic chips*** and accessories required for sample partitioning.” *Id.* at 5.

	’091 Claim Language	Infringement Support

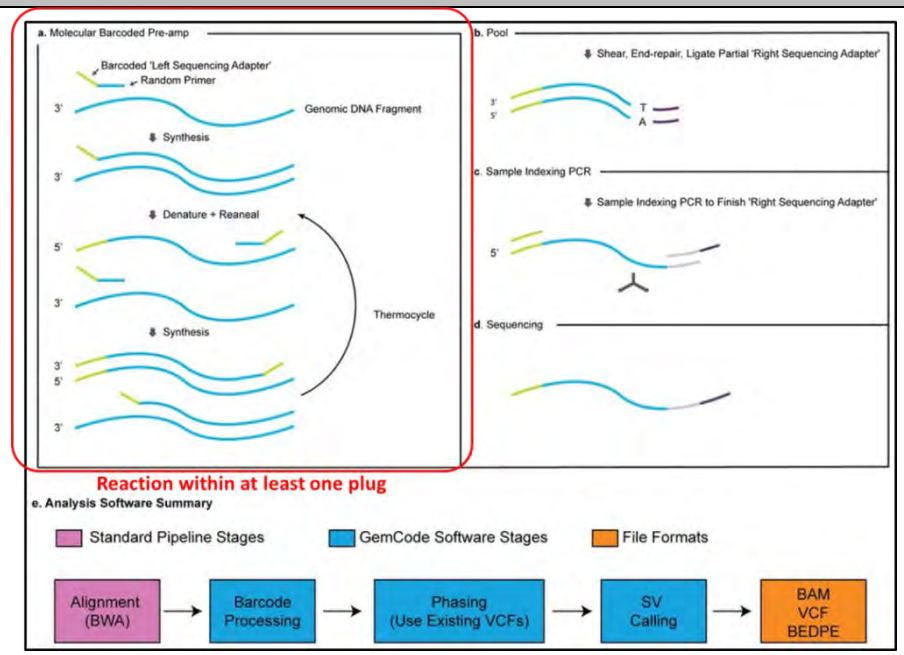


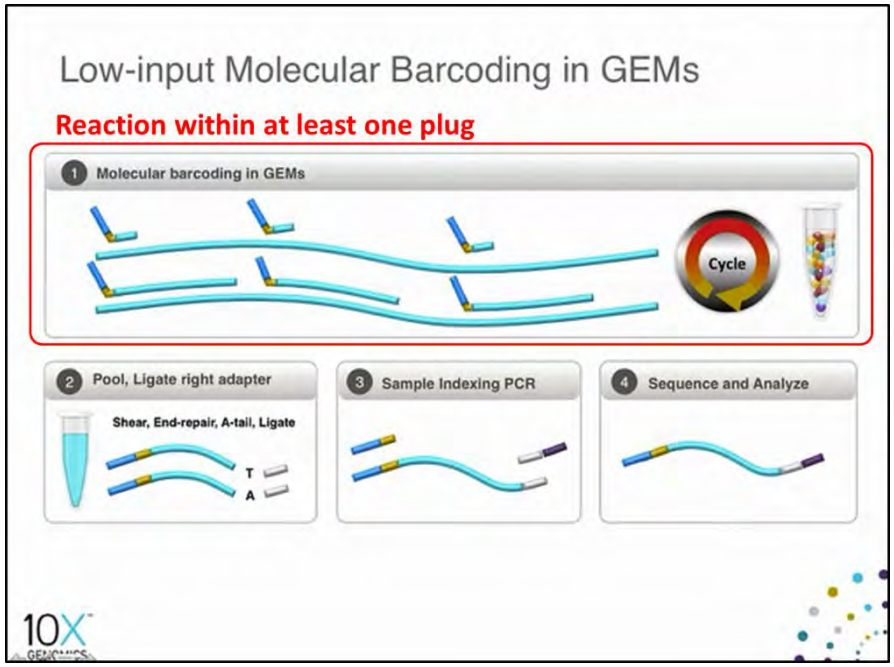
Id. at 1.

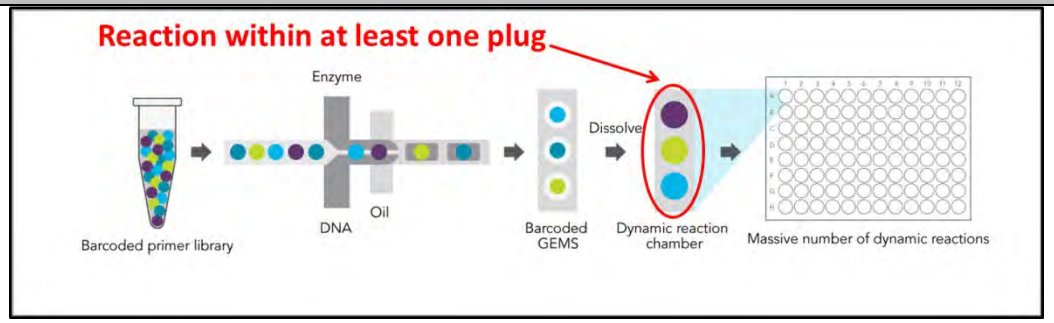
- 10x Technologies’ 2015 presentation at the JP Morgan healthcare conference further shows a microfluidic system for conducting reactions in plugs, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are the light gray circles in the rightmost channel.

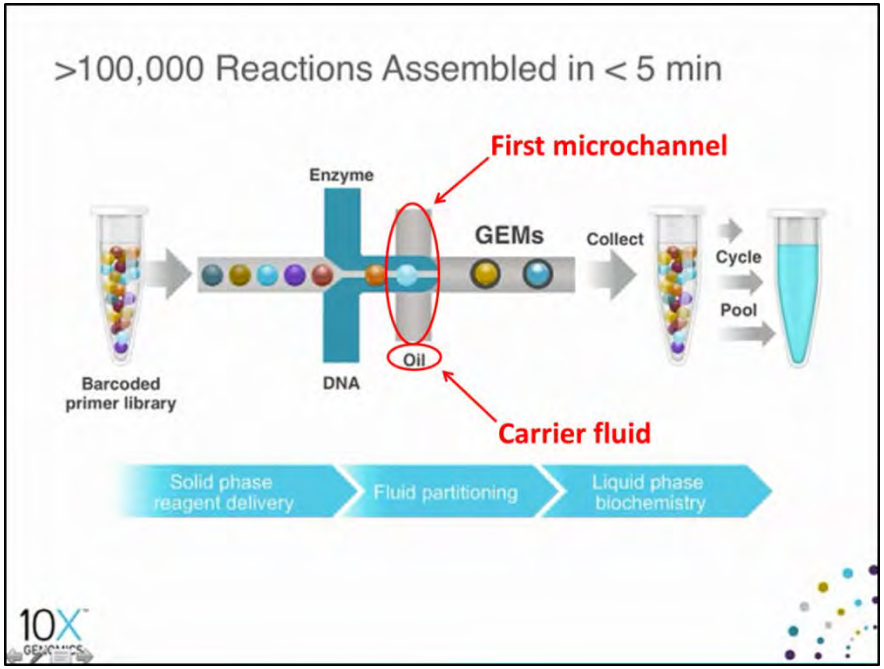


	'091 Claim Language	**Infringement Support**
		Ex. 37 [JP Morgan presentation] at 2. **<u>10X's GemCode platform conducts DNA amplification reactions within the microfluidic droplets ("plugs")</u>** • The slide above from 10X's August 2015 presentation is entitled ">100,000 ***Reactions*** Assembled in <5 min," which demonstrates that reactions are occurring within the microfluidic droplets. • The reactions which take place within the microfluidic droplets is depicted in the figure below in the panel labeled "a. Molecular Barcoded Pre-amp," which is taken from 10X's recent article in *Nature Biotechnology* that presents data based on the use of 10X's platform. The figure below shows a single stranded "Genomic DNA Fragment" that is extended through the use of a "Random Primer." The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process.

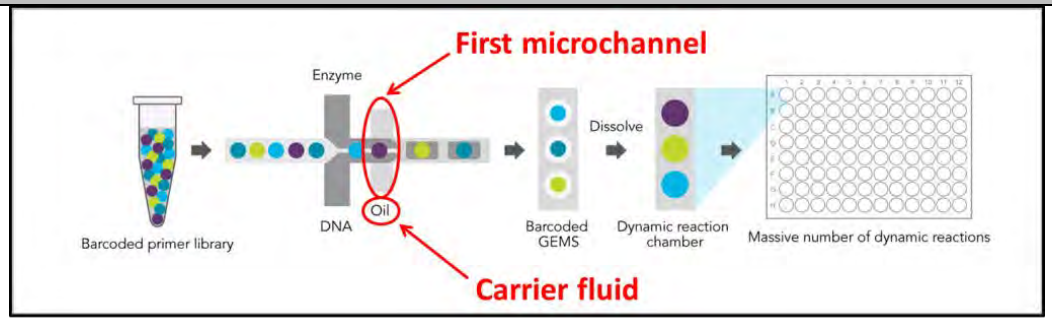
	’091 Claim Language	Infringement Support
		 Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X’s publication states, “1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes.” *Id.* at 3432. • During his August 2015 webinar, Dr. Schall-Levin also described the DNA amplification reaction that takes place in the droplets with reference to the figure below. “So now the biochemistry that’s happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you’ve broken the droplets and put everything back together in bulk. First you can concentrate on the top panel showing the biochemistry that’s happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal cycling protocol, oligos which have been released as***

	'091 Claim Language	Infringement Support
		the gel bead fall apart prime off of the genome and do a low-level of copying. The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template." Ex. 4 [10X Webinar] at 13:00-53.  • The figure below from 10x's website depicts the microfluidic system wherein plugs are received in a "dynamic reaction chamber" wherein a "massive number of dynamic reactions" occur.

	’091 Claim Language	Infringement Support
		 Ex. 39 [10X Website Excerpts] at 1.
091-36b	introducing a carrier-fluid into a first microchannel of a device;	10X’s GemCode platform provides “introducing a carrier-fluid into a first microchannel of a device.” • The carrier fluid is the oil. • The first microchannel is the channel that intersects perpendicularly with the central channel and that carries the oil. **10X’s GemCode platform introduces an oil (“carrier fluid”) into a first channel of a microfluidic chip.** • During his August webinar, Dr. Schnall-Levin explained that the picture below is “a cross-section of one of the ***channel in our microfluidic chip***.” *Id.* at 9:33-39. “If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And ***on the third input well the user puts in the oil provided again by 10X***. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead.”*** *Id.* at 9:48-10:39. Thus, the channel containing the oil (which is a “carrier fluid immiscible with the aqueous

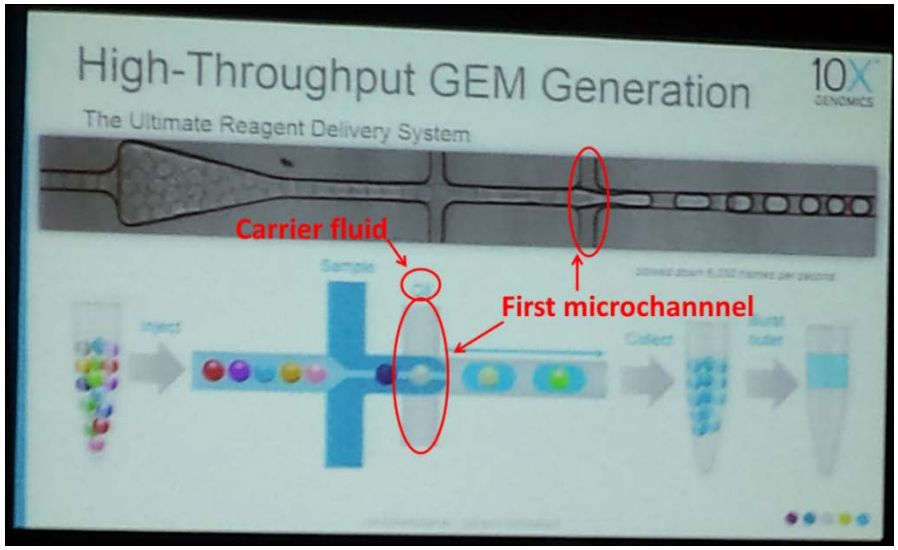
	’091 Claim Language	Infringement Support
		solutions”) intersects and flows into the channel containing the aqueous solution of the gel beads, biochemical reagents and DNA.  • In the figure above the channel containing the continuously flowing oil is shown in grey. • The figure below from 10x’s website further notes the continuously flowing oil from a second channel shown in light grey.

	’091 Claim Language	Infringement Support

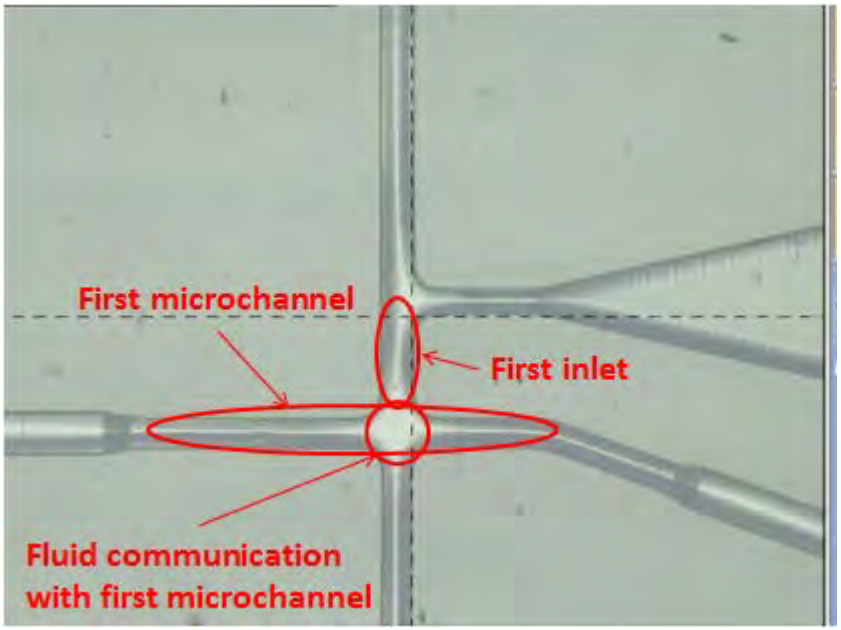


Ex. 39 [10X Website Excerpts] at 1.

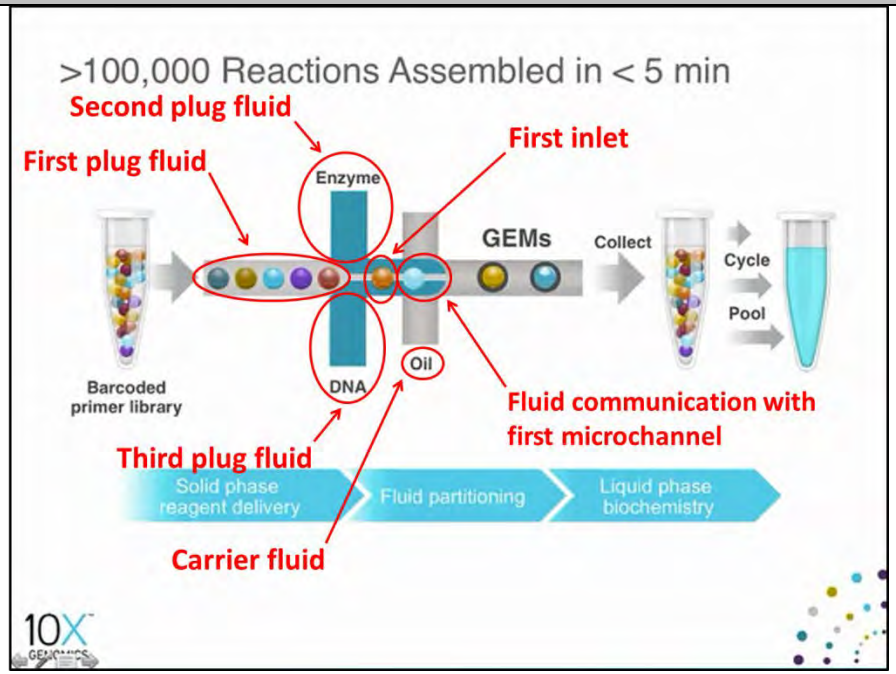
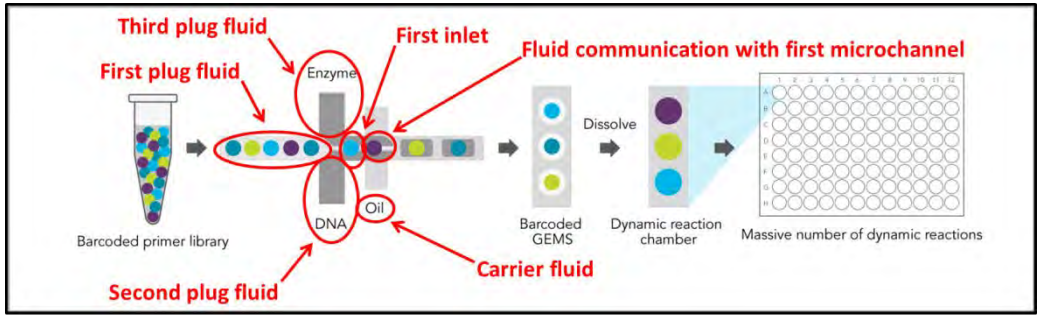
- Similarly, 10X’s 2015 JP Morgan presentation shows a microfluidic system through which an oil is shown flowing into a channel of the microfluidic chip in light grey:

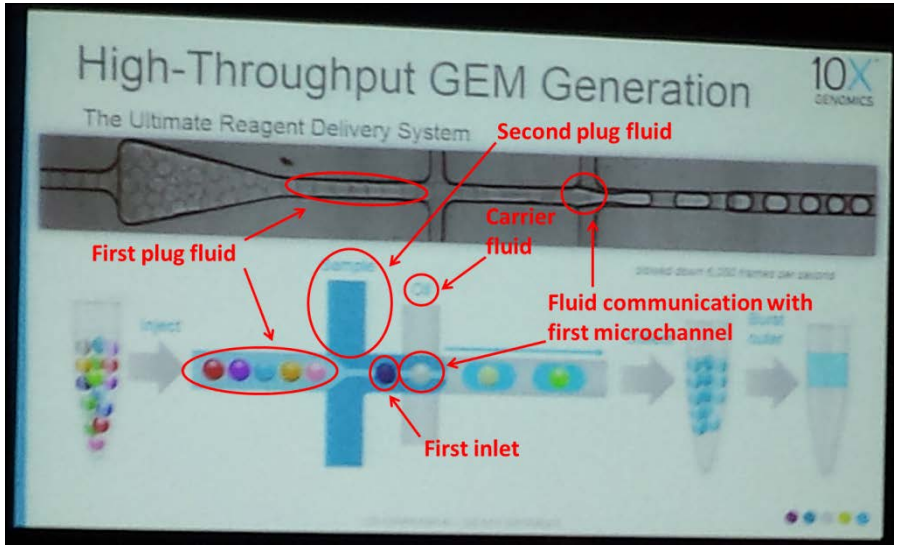


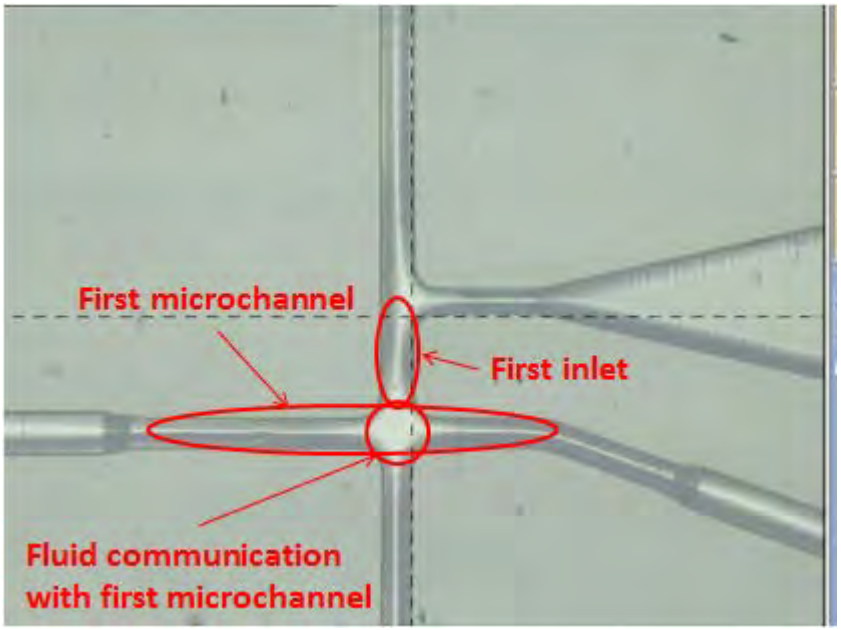
Ex. 37 [JP Morgan presentation] at 2.

	’091 Claim Language	Infringement Support
		• 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same inlet. This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. The oil carrier fluid is introduced into what has been labeled “first microchannel.” 
091-36c	simultaneously	10X’s GemCode platform “simultaneously introduc[es] at least two streams of plug-fluids into

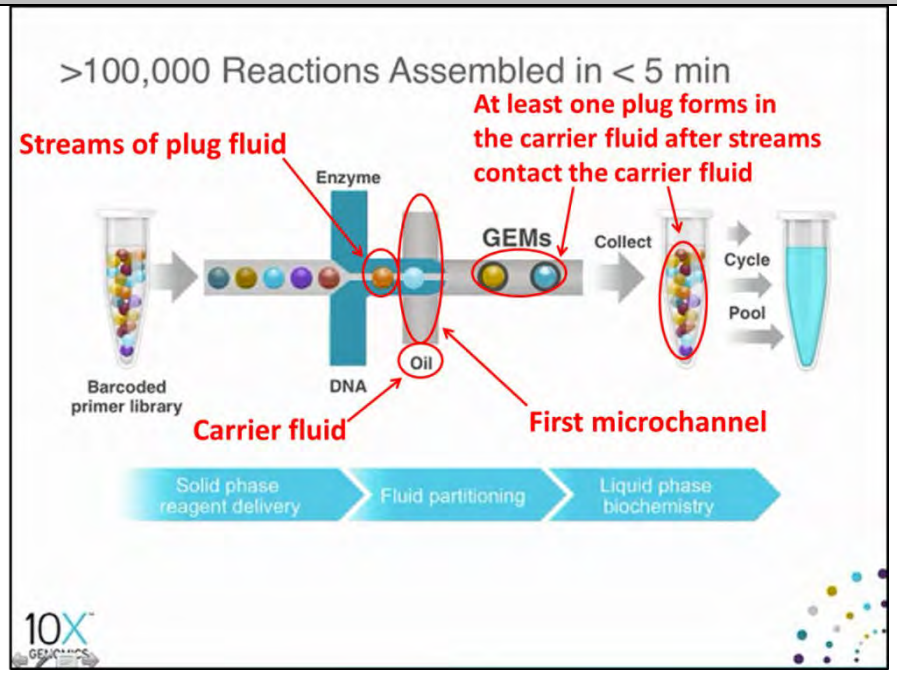
	'091 Claim Language	**Infringement Support**
	introducing at least two streams of plug-fluids into a first inlet in fluid communication with the first microchannel so that at least one plug forms in the carrier fluid at a junction of the first inlet and the first microchannel; wherein:	a first inlet in fluid communication with the first microchannel so that at least one plug forms in the carrier-fluid after the streams contact the carrier-fluid" • There are at least three streams of aqueous fluid in 10X's product: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads. Any two of these fluids may be chosen as the first and second plug fluid. The designations of the first, second, and third fluids in the figures in this chart are arbitrary. • The three plug fluids are introduced into an inlet that perpendicularly intersects (and is hence in fluid communication with) the first microchannel that carries the oil carrier fluid. • The plugs are the droplets (which 10X sometimes refer to as GEMs) that form at the junction between the inlet and the carrier fluid stream. **10X's GemCode platform simultaneously introduces three streams of plug fluid into a first inlet** • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is "a cross-section of one of the channels in our microfluidic chip." Ex. 4 [10X Webinar] at 9:33-39. "If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads.*** This is a reagent delivered by 10x. ***On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly***. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead." *Id.* at 9:48-10:39. Thus, two streams of plug-fluids, the first containing biochemical reagents and DNA, and the second containing an aqueous solution of the gel beads, are introduced into the same central inlet channel.

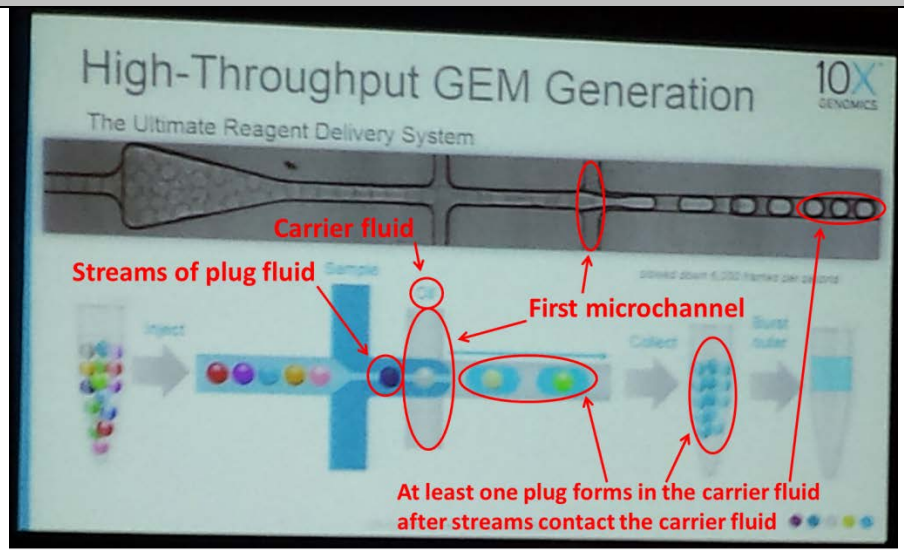
	’091 Claim Language	Infringement Support
		 • The figure below from 10x’s website further notes the introduction of two streams through a central channel. 

	’091 Claim Language	Infringement Support
		Ex. 39 [10X Website Excerpts] at 1. • Similarly, 10X’s 2015 JP Morgan presentation shows a microfluidic system through which two streams are introduced to a middle inlet channel.  Ex. 37 [JP Morgan presentation] at 2. • 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same inlet. This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. A first and second stream of plug fluid are introduced into

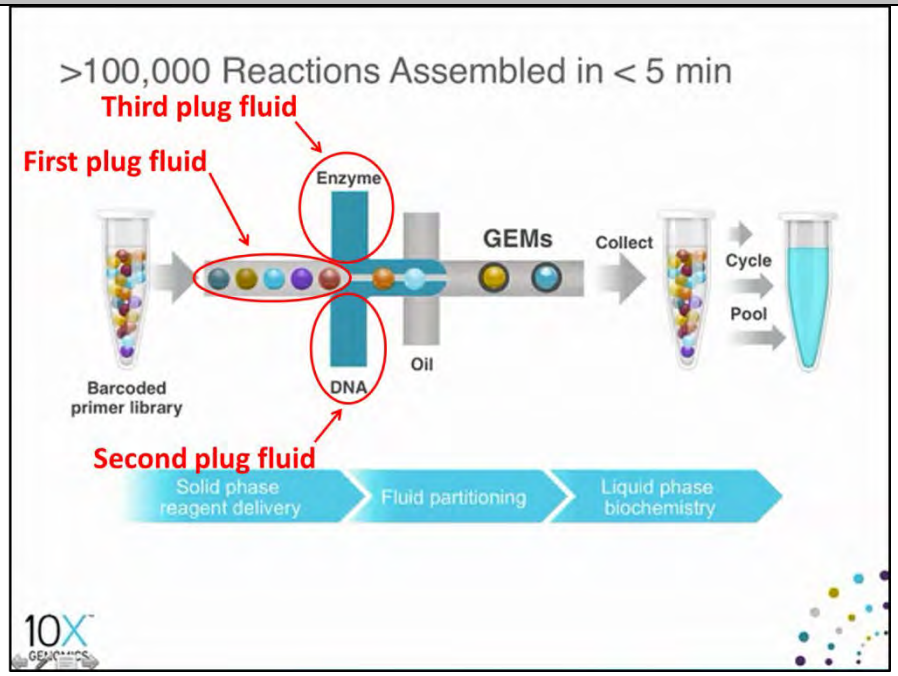
	’091 Claim Language	Infringement Support
		what is labeled “first inlet.” Those streams are in fluid communication with the “first microchannel.”  **The streams of plug fluid are in fluid communication with the first channel containing the oil (“carrier-fluid”) such that droplets (“plugs”) form in the oil at the junction between the first microchannel and the inlet** • The ’091 patent’s description of “plugs” includes the following: “‘Plugs’ in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible.” Ex. 11 [’091 patent] at 9:20-23.

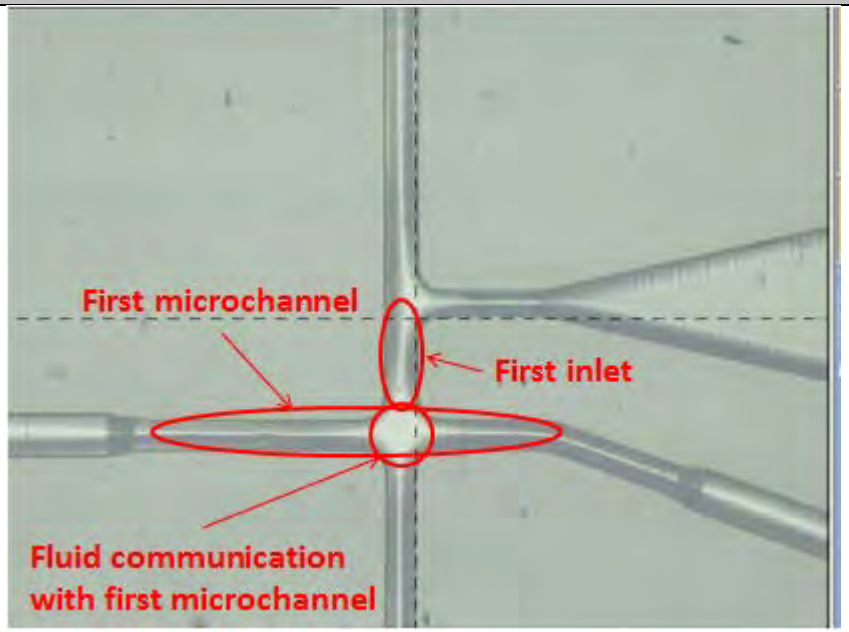
	'091 Claim Language	**Infringement Support**
		• On August 5, 2015, Michael Schnall-Levin, 10X's Vice President of Computational Biology and Applications, presented a webinar "about the GemCode platform." Ex. 4 [10X Webinar] at 3:17-3:23; *see also id.* at 3:35-38 ("I'm really excited today to take you through our Platform."). During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms plugs in the manner described by the '091 patent with reference to the below figure: "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." *Id.* at 9:48-10:39.

	’091 Claim Language	Infringement Support
		 • 10x Technologies’ 2015 presentation at the JP Morgan healthcare conference further shows that plugs are formed after the two inlet streams of plug fluid intersect the oil, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are the light gray circles in the rightmost channel.

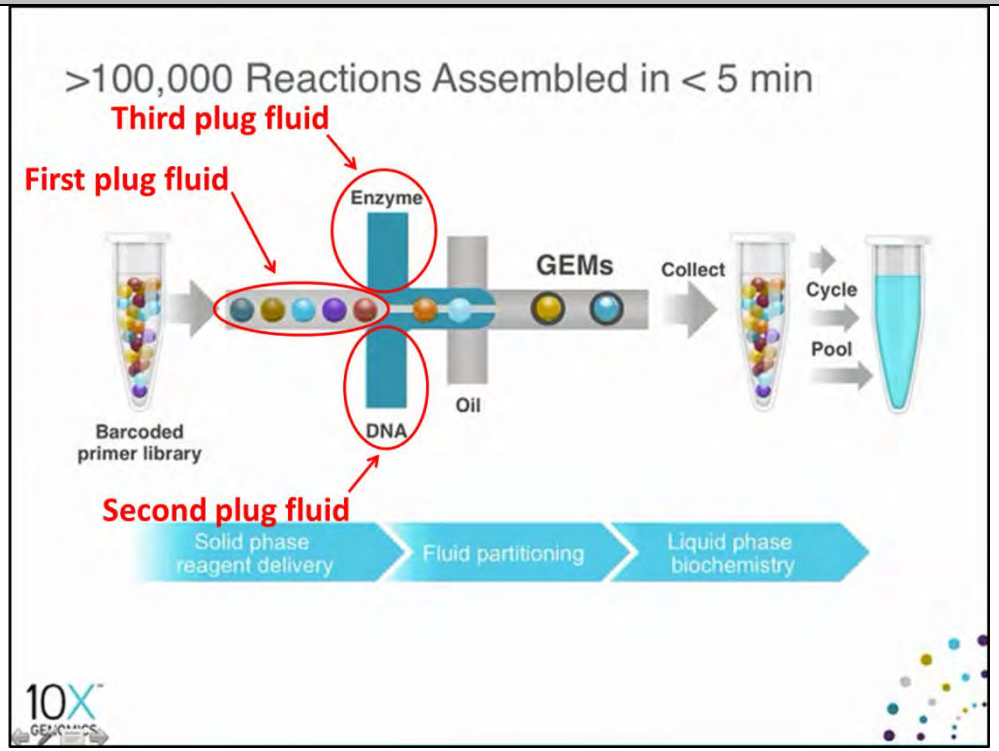
	'091 Claim Language	**Infringement Support**
		 Ex. 37 [JP Morgan presentation] at 2.
091-36d	-a first plug-fluid comprises a first reagent;	10X's GemCode platform has a first plug fluid that comprises a first reagent. • There are at least three streams of plug fluid in 10X's product that each contains one or more reagents: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads, which deliver primers. • The sample DNA is a substrate for a DNA amplification reaction. The enzyme is a reagent that catalyzes the amplification reaction, and is delivered with other reagents (e.g, nucleotides) that are used in the amplification reaction. The gel beads deliver primers that are used in the amplification reaction. • Any one of plug fluids comprising reagents may be designated as the first plug fluid comprising a first reagent. The designations of the first plug fluid, second plug fluid,

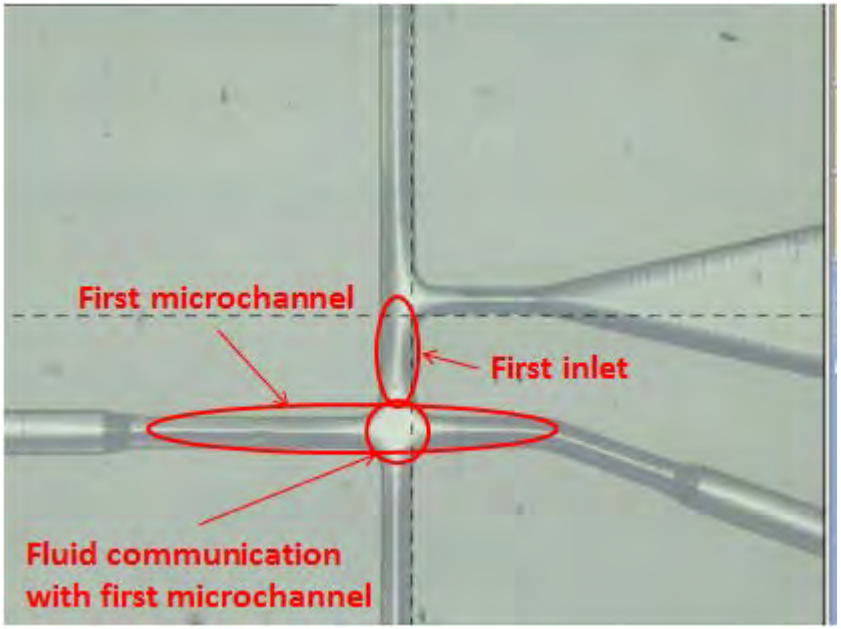
	’091 Claim Language	Infringement Support
		and third plug fluid in this chart are arbitrary. **<u>10X’s GemCode platform has at least three aqueous fluids that each contain one or more reagents.</u>** • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is “a cross-section of one of the channels in our microfluidic chip.” Ex. 4 [10X Webinar] at 9:33-39. “If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10x. On the second input well the user mixes our biochemical reagents with their DNA.*** And on the third input well the user puts in the oil provided again by 10X. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead.” *Id.* at 9:48-10:39.

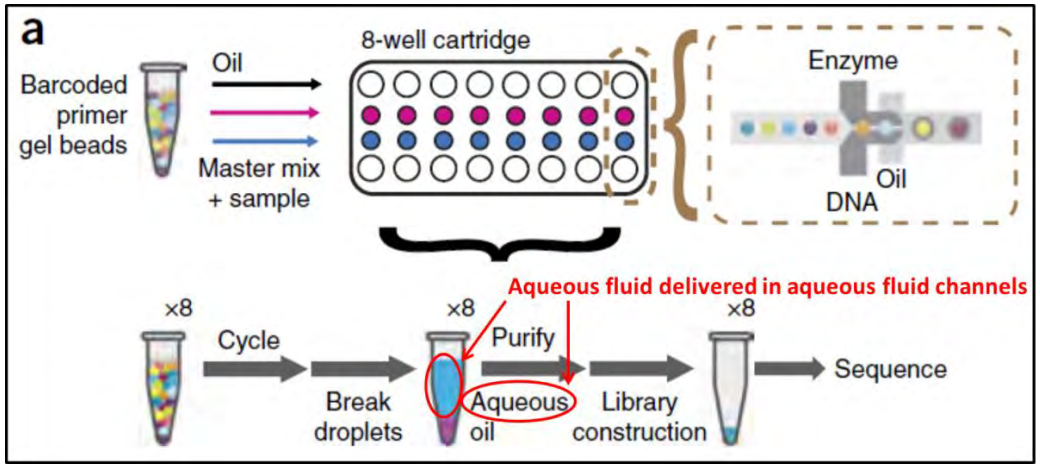
	’091 Claim Language	Infringement Support
		 • 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same inlet. This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. A first stream of plug fluid is introduced from the topmost channel and is comprised of one or more reagents.

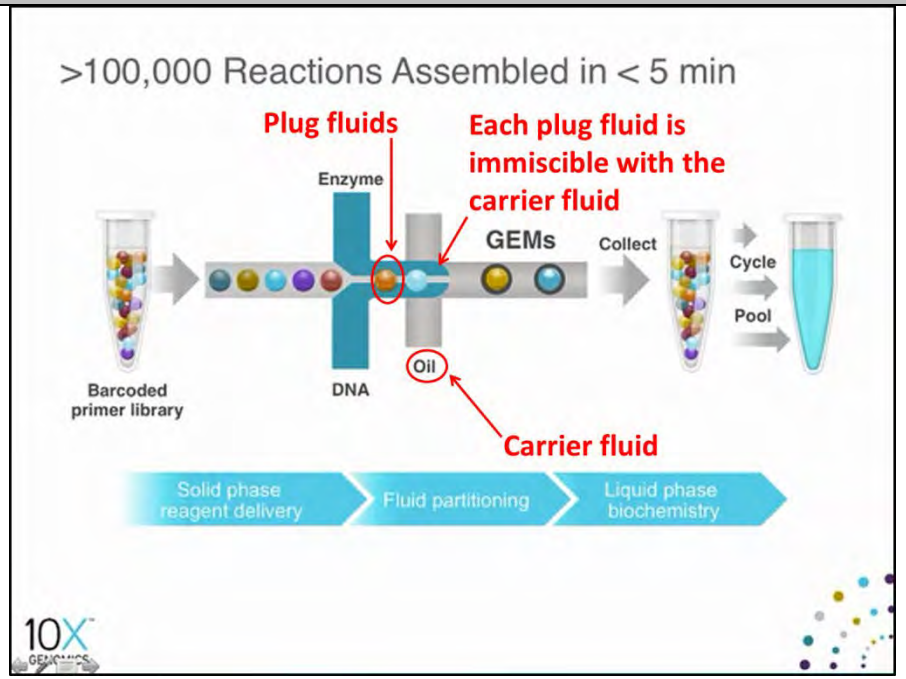
	'091 Claim Language	**Infringement Support**
		
091-36e	-a second plug-fluid comprises a second reagent different from the first reagent;	10X's GemCode platform has a second plug fluid that comprises a second reagent. • There are at least three streams of plug fluid in 10X's product that each contains one or more reagents: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads, which deliver primers. • The sample DNA is a substrate for a DNA amplification reaction. The enzyme is a reagent that catalyzes the amplification reaction, and is delivered with other reagents (e.g, nucleotides) that are used in the amplification reaction. The gel beads deliver primers that are used in the amplification reaction. • Any one of plug fluids comprising reagents may be designated as the second plug fluid comprising a second reagent, consistent with the choice that is made for the first plug fluid and reagent. The designations of the first plug fluid, second plug fluid, and third

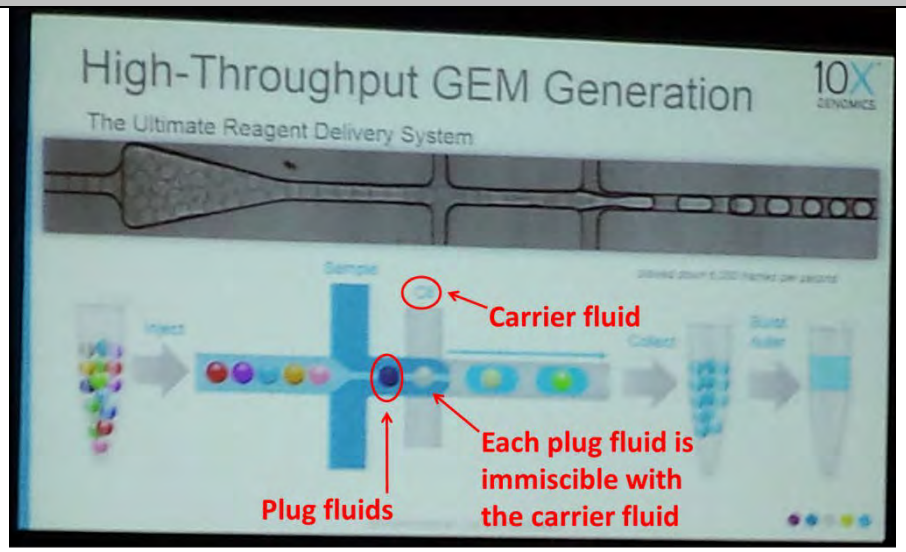
	’091 Claim Language	Infringement Support
		plug fluid in this chart are arbitrary. **<u>10X’s GemCode platform has at least three aqueous fluids that each contain one or more reagents.</u>** • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is “a cross-section of one of the channels in our microfluidic chip.” Ex. 4 [10X Webinar] at 9:33-39. “If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10x***. ***On the second input well the user mixes our biochemical reagents with their DNA.*** And on the third input well the user puts in the oil provided again by 10X. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead.” *Id.* at 9:48-10:39.

	’091 Claim Language	Infringement Support
		 • 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same inlet. This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. A second stream of plug fluid is introduced from the top right channel and is comprised of one or more reagents that are different from the reagents in the first stream of plug fluid.

	’091 Claim Language	Infringement Support
		
091-36f	-each plug-fluid is immiscible with the carrier-fluid; and	**The three plug fluids in 10X’s GemCode platform are aqueous and hence immiscible with the oil carrier fluid.** • In 10x’s GemCode platform the channels that carry the enzyme, DNA, and barcoded gelbeads for packaging into droplets are aqueous fluid channels. This is shown in 10X’s recent *Nature Biotechnology* paper, which describes the operation of 10X’s GemCode platform. As explained in this paper, “[t]he first junction combines a close-packed ***aqueous*** slurry of gel beads with the sample and reagent mixture, and the second junction delivers the oil-surfactant solution.” Ex. 5 [*Nature Biotechnology*] at 2. The droplets that are formed in 10X’s microfluidic device are broken after a DNA amplification reaction is carried out inside the droplet. The fluid that is inside the droplets separates from the oil that originally surrounded and carried the droplets. As

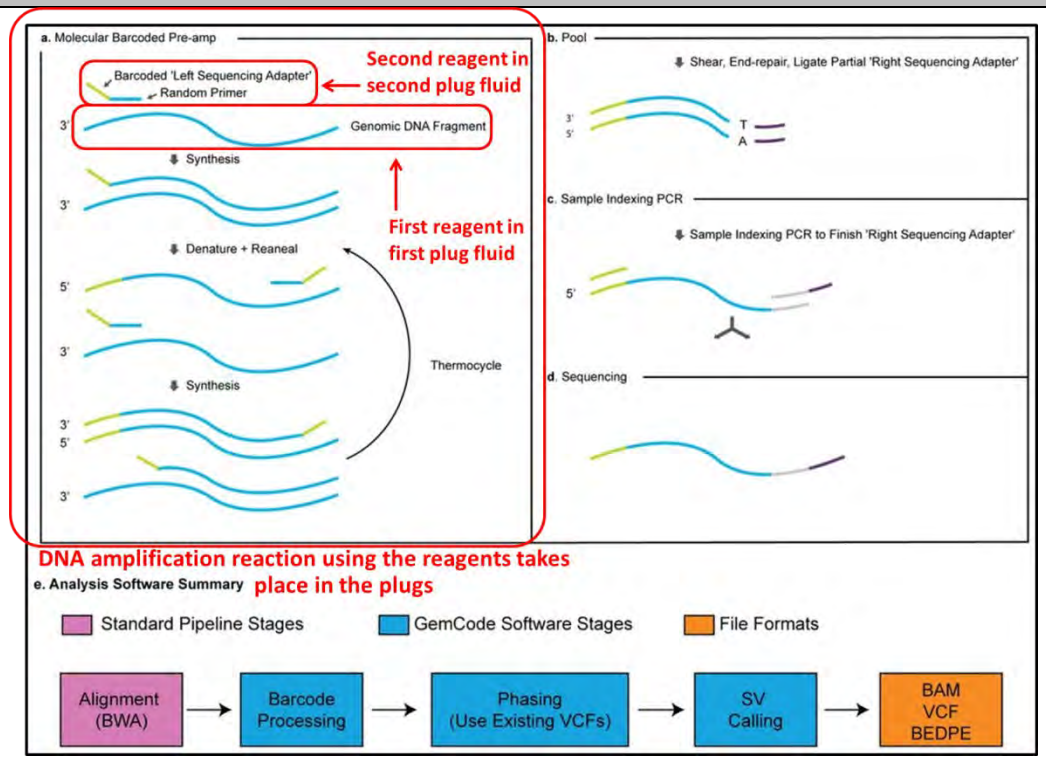
	’091 Claim Language	Infringement Support
		depicted below, the interior of the droplet is “Aqueous” and is shown in blue. Thus, the channels that provided the fluids for the interior of the droplets are aqueous fluid channels.  Ex. 5 [*Nature Biotechnology*] at Fig. 1a. • During his August 2015 presentation, Dr. Schnall-Levin described how 10X’s microfluidic device forms plugs in the manner described by the ‘091 patent with reference to the below figure: “If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***.” Ex. 4 [10X Webinar] at 9:48-10:39.

	’091 Claim Language	Infringement Support
		 • As shown in the above image, the blue fluid and colored gel beads are immiscible with the oil because the intersection forms isolated droplets rather than a homogenous liquid. • 10x Technologies’ 2015 presentation at the JP Morgan healthcare conference further shows that the plug fluids are immiscible with the oil, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are created after introducing the plug-fluid liquids to the microchannel containing the flow of oil.

	'091 Claim Language	**Infringement Support**
		 Ex. 37 [JP Morgan presentation] at 2.
091-36g	-each plug comprises both the first and second plug-fluids so that the reaction of the reagents substantially occurs in the plug;	In 10X's GemCode platform "each plug comprises both the first and second plug-fluids so that the reaction of the reagents substantially occurs in the plug." • There are at least three streams of plug fluid in 10X's GemCode platform: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads, which deliver primers. All of these plug fluids are packaged into droplets, and any two of these plug fluids may be selected as the first and second plug fluid. • The reaction that occurs in the droplets using the reagents contained in the plug fluids is a DNA amplification reaction. **<u>The microfluidic droplets ("plugs") in 10X's GemCode platform comprise all three of the plug fluids that are used in 10X's product.</u>** • During his August 2015 presentation, Dr. Schnall-Levin explained that each droplet

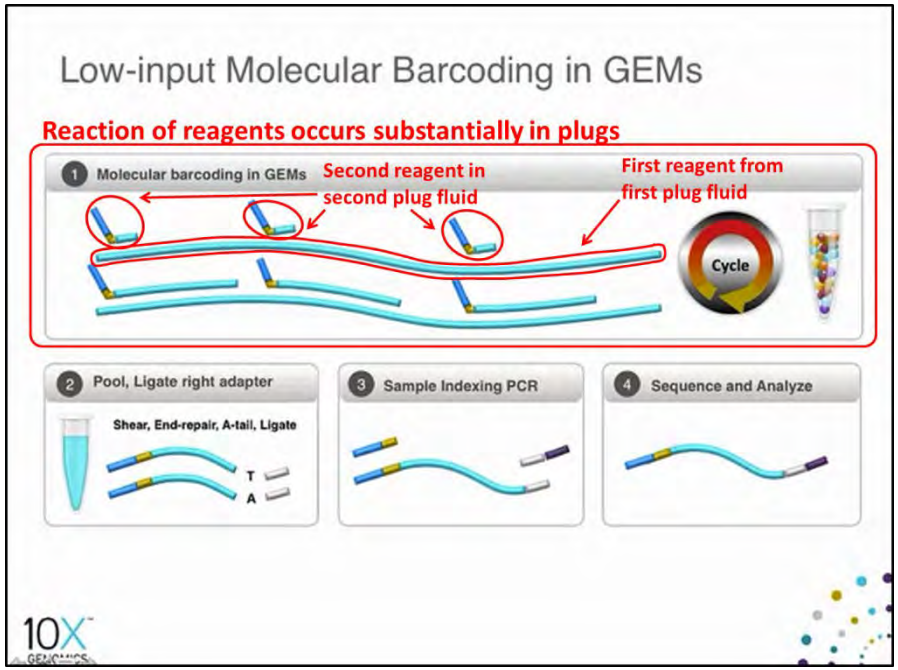
	'091 Claim Language	**Infringement Support**
		contains a small portion of the DNA from the user and a gel bead: "If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA.*** And on the third input well the user puts in the oil provided again by 10X. ***There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." Ex. 4 [10X Webinar] at 9:48-10:39. **10X's GemCode platform conducts DNA amplification reactions within the microfluidic droplets ("plugs") using the reagents from the first and second plug fluids** • The reactions which take place within the microfluidic droplets is depicted in the figure below in the panel labeled "a. Molecular Barcoded Pre-amp," which is taken from 10X's recent article in *Nature Biotechnology* that presents data based on the use of 10X's platform. The figure below shows a single stranded "Genomic DNA Fragment" that is extended through the use of a "Random Primer." The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process.

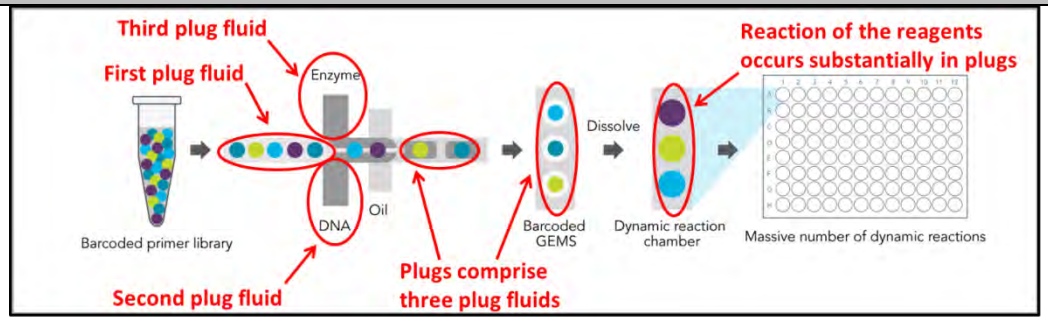
	’091 Claim Language	Infringement Support

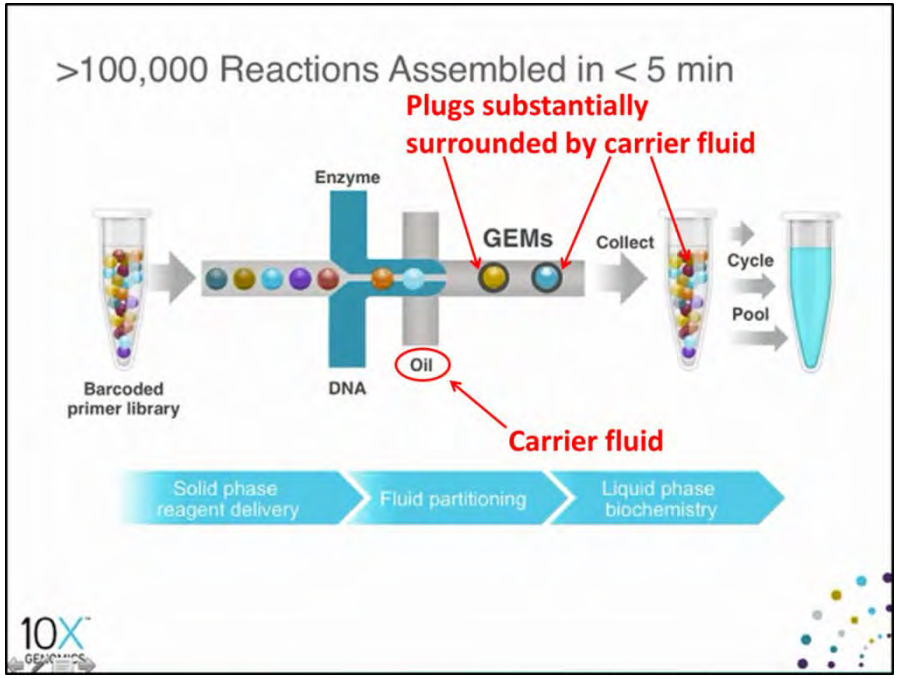


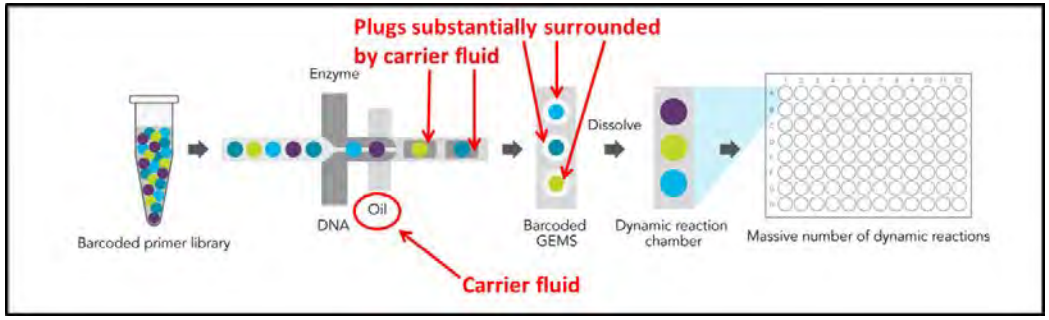
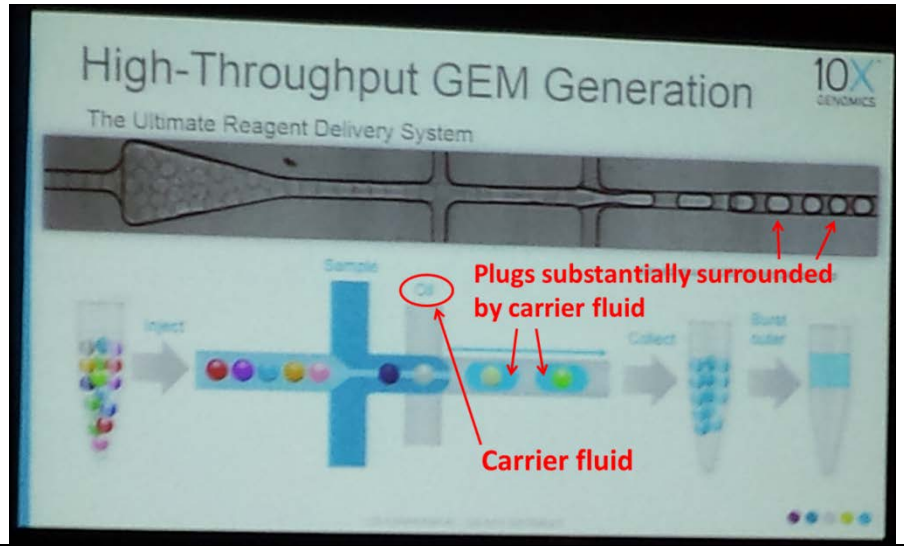
Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X’s publication states, “1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes.” *Id.* at 3432.

- During his August 2015 webinar, Dr. Schall-Levin also described the DNA amplification reaction that takes place in the droplets with reference to the figure below. “So now the biochemistry that’s happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you’ve broken the droplets and put everything back together in bulk. First you can concentrate on the top panel showing the biochemistry

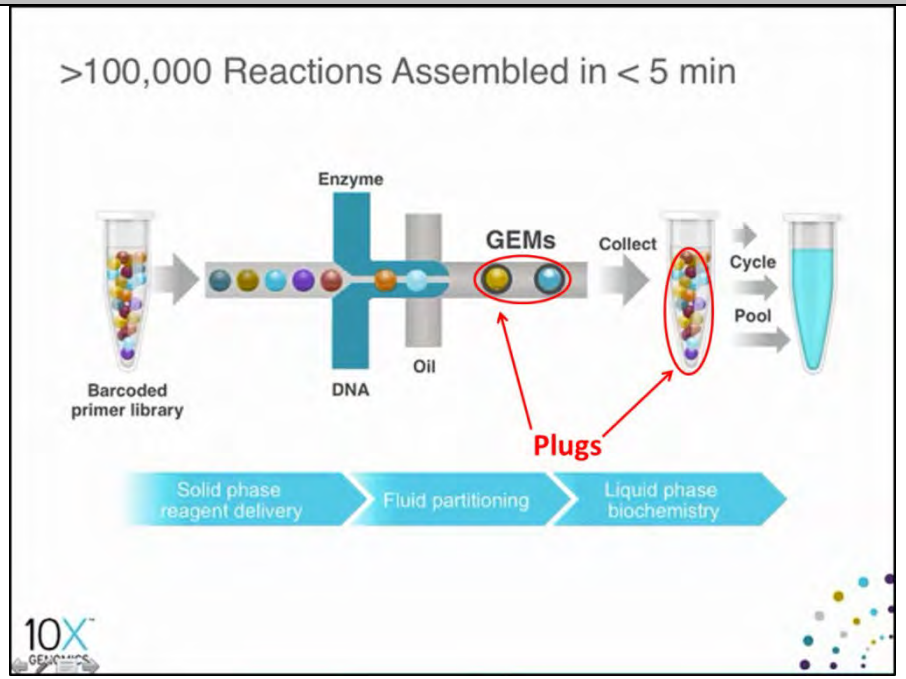
	'091 Claim Language	Infringement Support
		that's happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying.*** The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template." Ex. 4 [10X Webinar] at 13:00-53.  • The figure below from 10x's website depicts the microfluidic system wherein plugs are received in a "dynamic reaction chamber" wherein a "massive number of dynamic reactions" occur.

	’091 Claim Language	Infringement Support
		 *Id.* at 1.
091-36h	-each plug is substantially surrounded by carrier.	**10X’s GemCode platform forms microfluidic droplets (“plugs”) such that the droplets are substantially surrounded by the oil.** • The ‘091 patent’s description of “plugs” includes the following: “‘Plugs’ in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible.” Ex. 11 [’091 patent] at 9:20-23. • During his August 2015 presentation, Dr. Schnall-Levin described how 10X’s microfluidic device forms plugs in the same manner as the ’091 patent. The process is depicted in the figure below. “If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***.” Ex. 4 [10X Webinar] at 9:48-10:39.

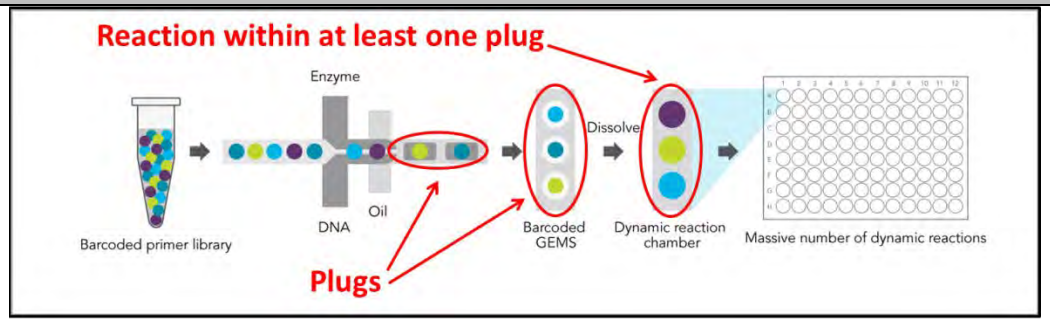
	’091 Claim Language	Infringement Support
		 • As shown in the image above, each microfluidic droplet or plug is called a “GEM” and is substantially surrounded by the grey oil, which is the carrier fluid. The partitioning of DNA into droplets by 10X’s GemCode system according to the foregoing methods is also established by other resources. For instance, 10x’s website states “The 10X Genomics reagent delivery system randomly partitions DNA fragments, then prepares sequencing libraries in parallel such that all molecules produced within a partition share a unique, partition-specific barcode.” Ex. 39 [10x Website Excerpts] at 1. The website further states that the 10x chip kit “[c]ontains the microfluidic chips and accessories required for ***sample partitioning***.” *Id.* at 5. 10x’s website further shows the formation of the claimed plugs:

	’091 Claim Language	Infringement Support
		 *Id.* at 1. • 10x Technologies’ JP Morgan presentation further shows the plugs emerging from the junction of the oil (shown in gray) and the aqueous fluid containing the reagents (shown in blue): 

	'091 Claim Language	**Infringement Support**
		Ex. 37 [JP Morgan presentation] at 2.
091-37a	37. A method of conducting a reaction within at least one plug comprising the steps of:	10X's GemCode platform uses "method of conducting a reaction within at least one plug." • The plugs are microfluidic droplets that are formed in 10X's GemCode platform. • A reaction that is conducted in the plug is a DNA amplification reaction. **10X's GemCode platform is a microfluidic system using "plugs," which 10X refers to as droplets or "GEMs".** • The '091 patent's description of "plugs" includes the following: "'Plugs' in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible." Ex. 11 ['091 patent] at 9:20-23. • On August 5, 2015, Michael Schnall-Levin, 10X's Vice President of Computational Biology and Applications, presented a webinar "about the GemCode platform." Ex. 4 [10X Webinar] at 3:17-3:23; *see also id.* at 3:35-38 ("I'm really excited today to take you through our Platform."). During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms plugs in the manner described by the '091 patent with reference to the below figure: "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." *Id.* at 9:48-10:39.

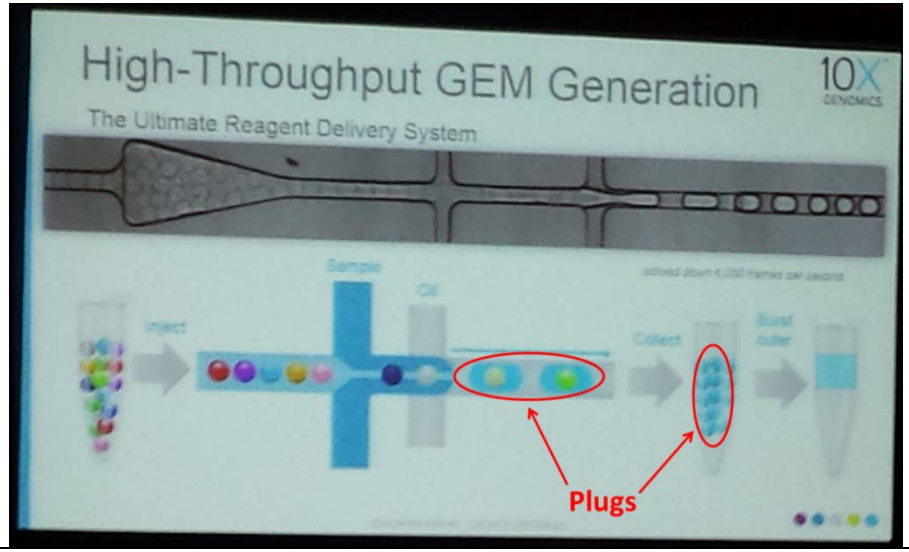
	’091 Claim Language	Infringement Support
		 • 10x’s website is consistent with Dr. Schnall-Levin’s description of 10X’s Platform. 10X’s website states that “[t]he instrument features precise ***microfluidics*** coupled with single button, user-friendly operation.” Ex. 39 [10X Website Excerpts] at 3. The website further states that the 10X chip kit “[c]ontains the ***microfluidic chips*** and accessories required for sample partitioning.” *Id.* at 5.

	’091 Claim Language	Infringement Support

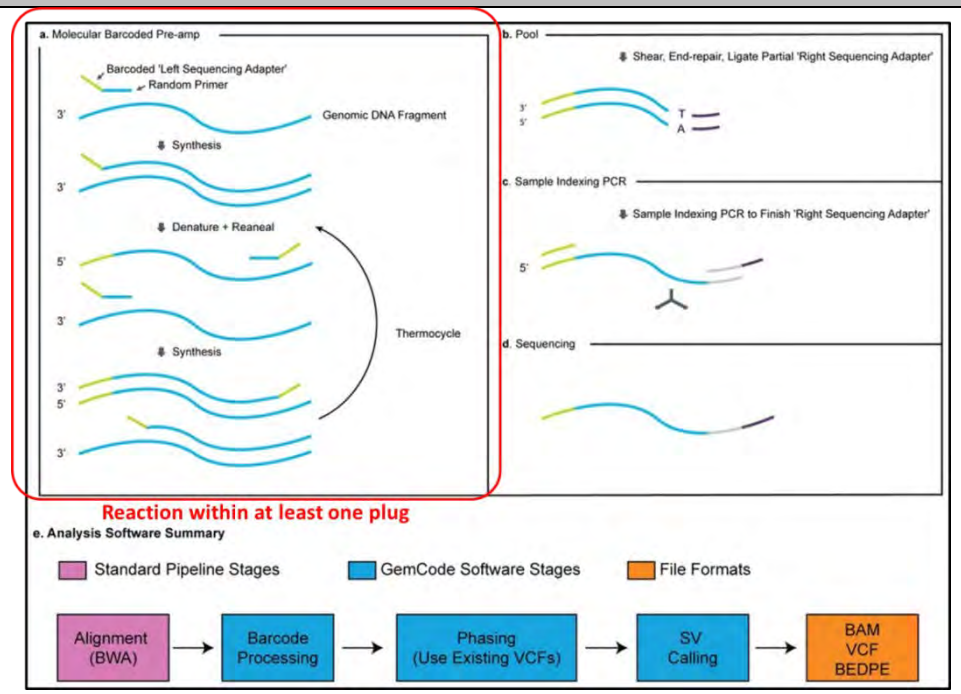


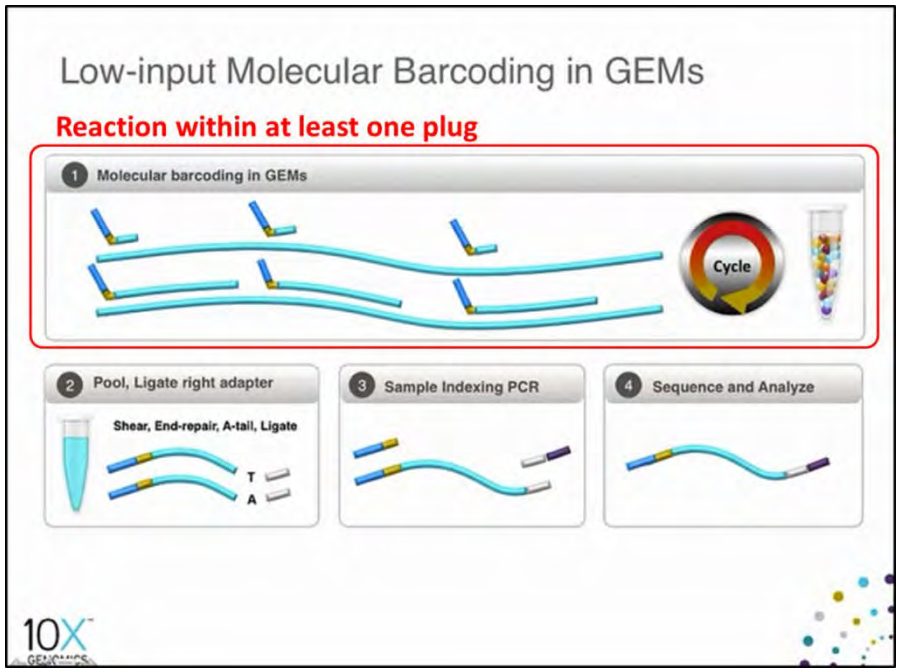
Id. at 1.

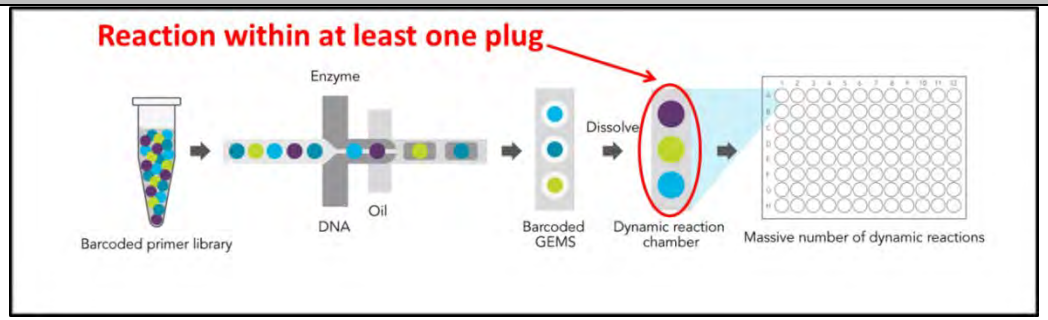
- 10x Technologies’ 2015 presentation at the JP Morgan healthcare conference further shows a microfluidic system for conducting reactions in plugs, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are the light gray circles in the rightmost channel.

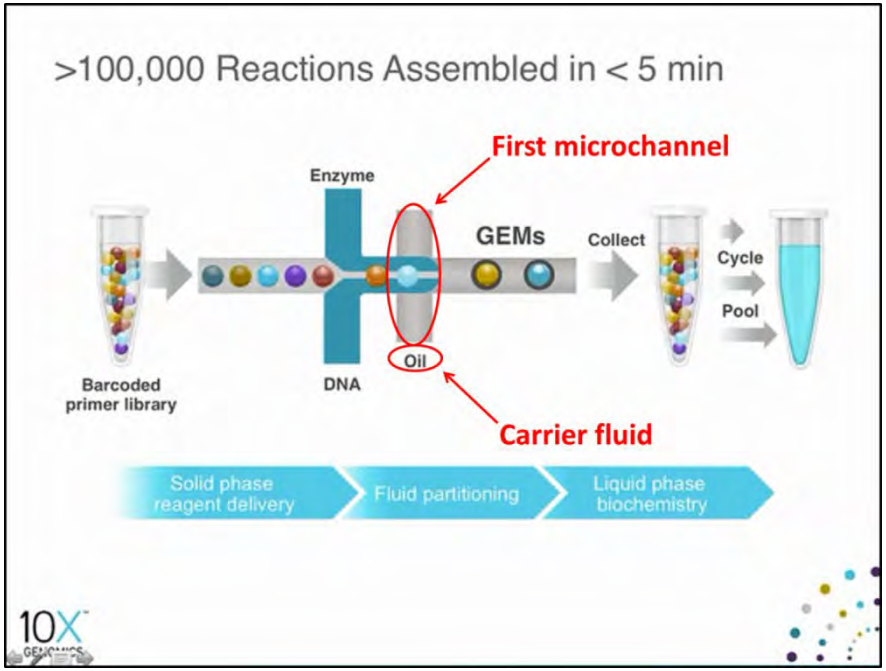


	'091 Claim Language	**Infringement Support**
		Ex. 37 [JP Morgan presentation] at 2. **<u>10X's GemCode platform conducts DNA amplification reactions within the microfluidic droplets ("plugs")</u>** • The slide above from 10X's August 2015 presentation is entitled ">100,000 ***Reactions*** Assembled in <5 min," which demonstrates that reactions are occurring within the microfluidic droplets. • The reactions which take place within the microfluidic droplets is depicted in the figure below in the panel labeled "a. Molecular Barcoded Pre-amp," which is taken from 10X's recent article in *Nature Biotechnology* that presents data based on the use of 10X's platform. The figure below shows a single stranded "Genomic DNA Fragment" that is extended through the use of a "Random Primer." The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process.

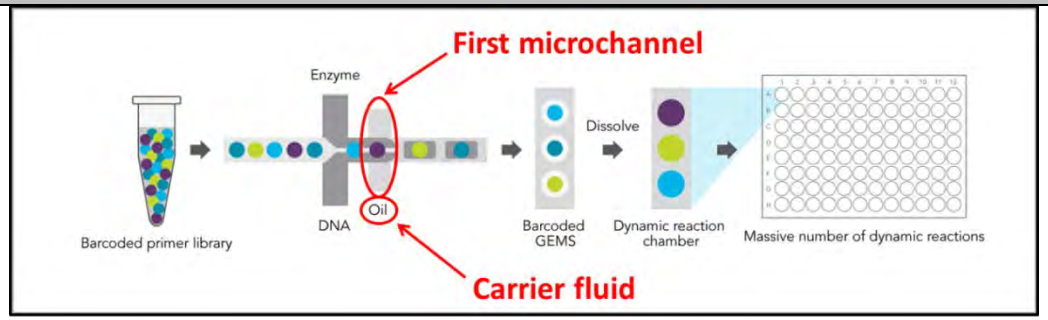
	’091 Claim Language	Infringement Support
		 Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X’s publication states, “1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes.” *Id.* at 3432. • During his August 2015 webinar, Dr. Schall-Levin also described the DNA amplification reaction that takes place in the droplets with reference to the figure below. “So now the biochemistry that’s happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you’ve broken the droplets and put everything back together in bulk. First you can concentrate on the top panel showing the biochemistry that’s happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling

	’091 Claim Language	Infringement Support
		protocol. ***During this thermal cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying.*** The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template.” Ex. 4 [10X Webinar] at 13:00-53.  • The figure below from 10x’s website depicts the microfluidic system wherein plugs are received in a “dynamic reaction chamber” wherein a “massive number of dynamic reactions” occur.

	’091 Claim Language	Infringement Support
		 Ex. 39 [10X Website Excerpts] at 1.
091-37b	introducing a carrier-fluid into a first microchannel of a device;	10X’s GemCode platform provides “introducing a carrier-fluid into a first microchannel of a device.” • The carrier fluid is the oil that is used in 10X’s microfluidic device. • The first microchannel is the channel through which the stream of oil is introduced perpendicularly into a stream of aqueous fluid that is packaged into droplets. **10X’s GemCode platform introduces an oil (“carrier fluid”) into a first channel of a microfluidic chip.** • During his August webinar, Dr. Schnall-Levin explained that the picture below is “a cross-section of one of the ***channel in our microfluidic chip***.” *Id.* at 9:33-39. “If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And ***on the third input well the user puts in the oil provided again by 10X***. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead.”*** *Id.* at 9:48-10:39. Thus, the channel containing the oil (which is a “carrier fluid immiscible with the aqueous

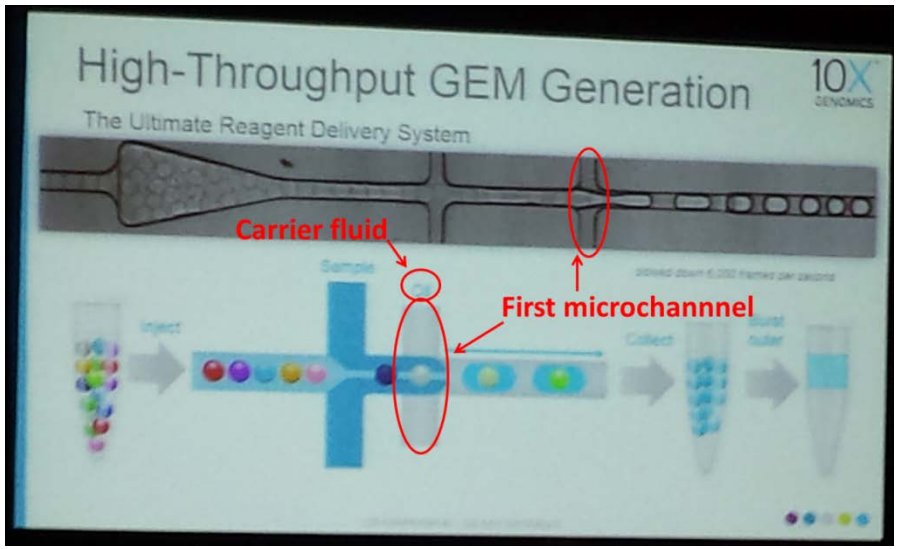
	’091 Claim Language	Infringement Support
		solutions”) intersects and flows into the channel containing the aqueous solution of the gel beads, biochemical reagents and DNA.  • In the figure above the channel containing the continuously flowing oil is shown in grey. • The figure below from 10x’s website further notes the continuously flowing oil from a second channel shown in light grey.

	’091 Claim Language	Infringement Support

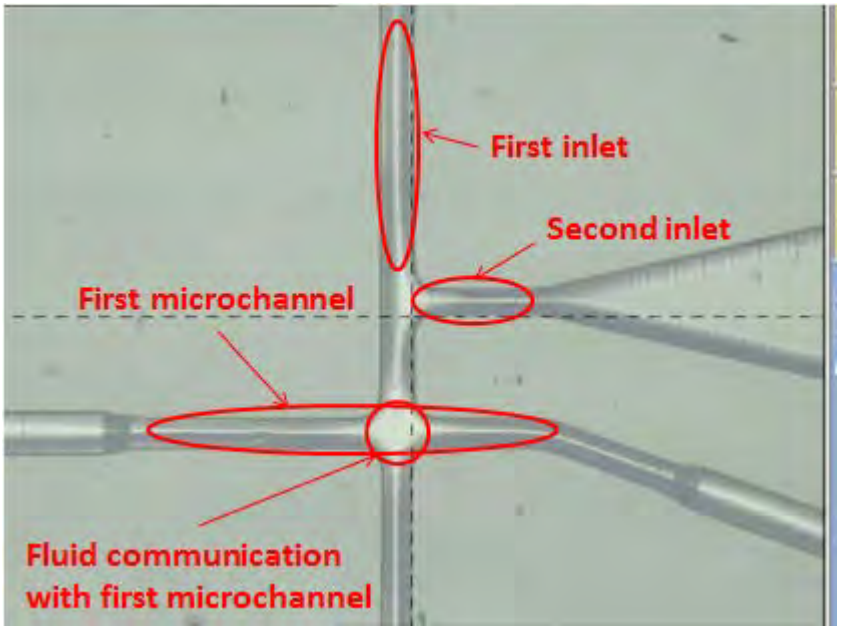


Ex. 39 [10X Website Excerpts] at 1.

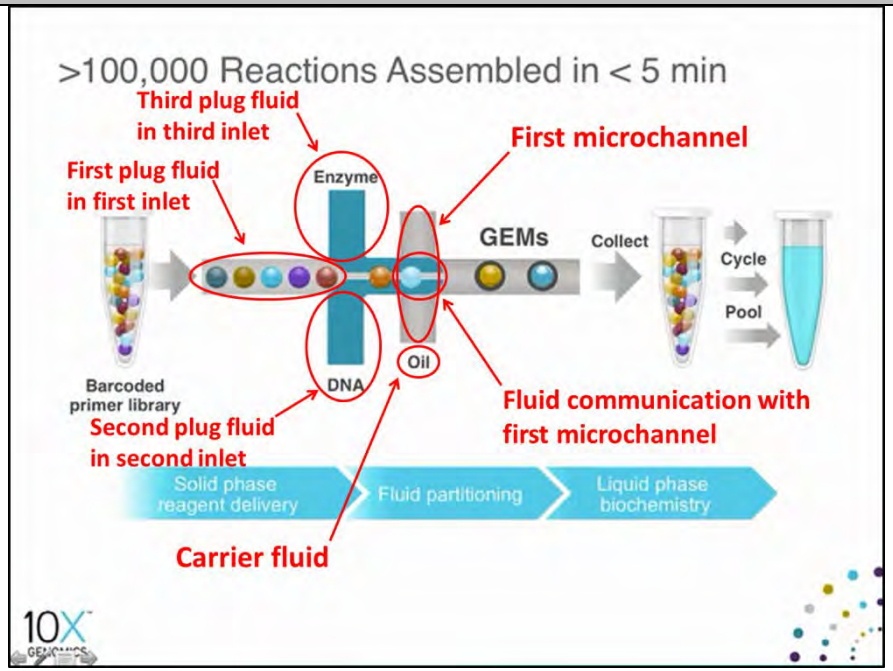
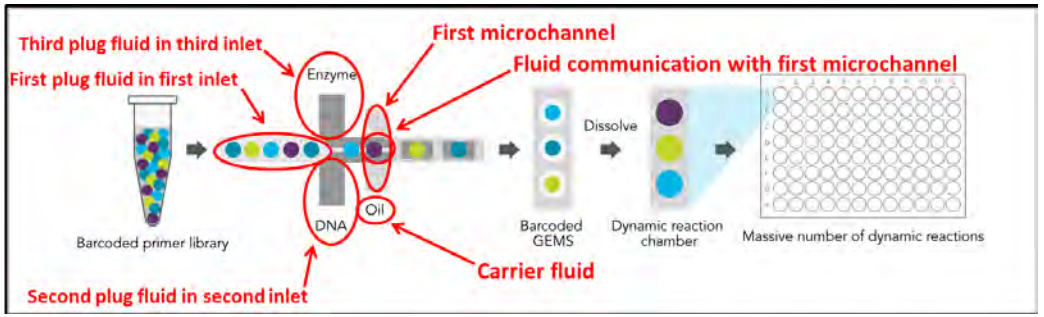
- Similarly, 10X’s 2015 JP Morgan presentation shows a microfluidic system through which an oil is shown flowing into a channel of the microfluidic chip in light grey:

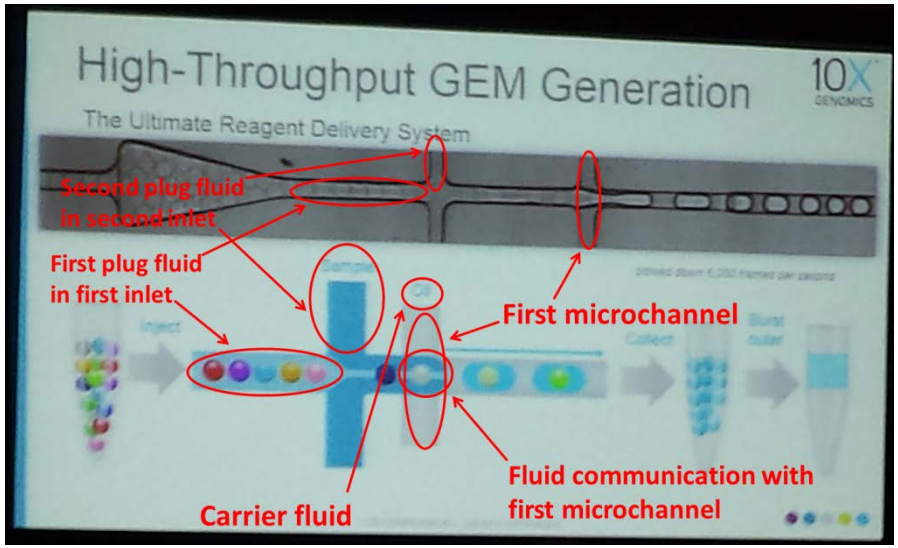


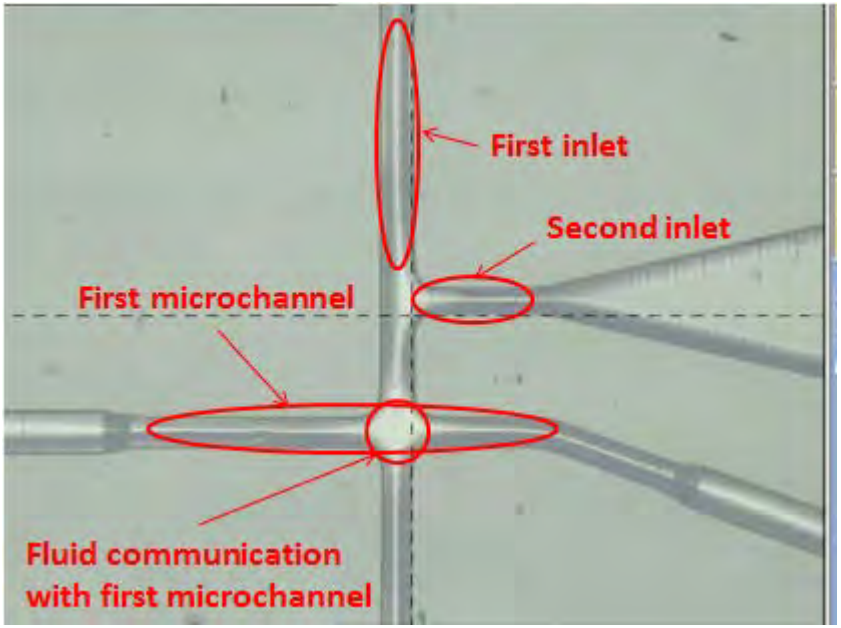
Ex. 37 [JP Morgan presentation] at 2.

	'091 Claim Language	**Infringement Support**
		• 10X's GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X's product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same inlet. This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. The oil carrier fluid is introduced into what is labeled "first microchannel." 
091-37c	introducing a stream of a first plug-fluid into a first	10X's GemCode platform introduces "a stream of a first plug-fluid into a first inlet in fluid communication with the first microchannel and simultaneously introducing a stream of a

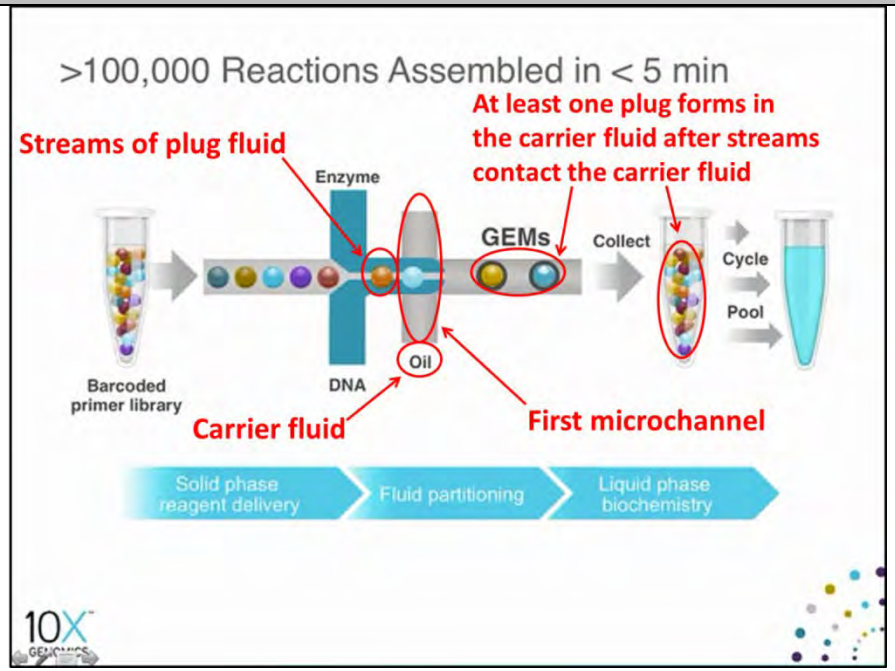
	'091 Claim Language	**Infringement Support**
	inlet in fluid communication with the first microchannel and simultaneously introducing a stream of a second plug-fluid into a second inlet in fluid communication with the first microchannel so that at least one plug forms in the carrier-fluid after the first and second plug-fluids contact the carrier fluid; wherein:	second plug-fluid into a second inlet in fluid communication with the first microchannel so that at least one plug forms in the carrier-fluid after the first and second plug-fluids contact The carrier fluid" • There are at least three streams of aqueous fluid in 10X's product: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads. Any two of these fluids may be chosen as the first and second plug fluid. The designations of the first, second, and third fluids in the figures in this chart are arbitrary. • Each of these three plug fluids are introduced via their own inlet. They combine at another inlet that perpendicularly intersects (and is hence in fluid communication with) the first microchannel that carries the oil carrier fluid. • The plugs are the droplets (which 10X sometimes refer to as GEMs) that form at the junction between the inlet and the carrier fluid stream. **10X's GemCode platform simultaneously introduces at least two streams of plug fluid via at least two inlets** • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is "a cross-section of one of the channels in our microfluidic chip." Ex. 4 [10X Webinar] at 9:33-39. "If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads.*** This is a reagent delivered by 10x. ***On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly***. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead." *Id.* at 9:48-10:39. Thus, two streams of plug-fluids, the first containing biochemical reagents and DNA, and the second containing an aqueous solution of the gel beads, are introduced into the same central inlet channel.

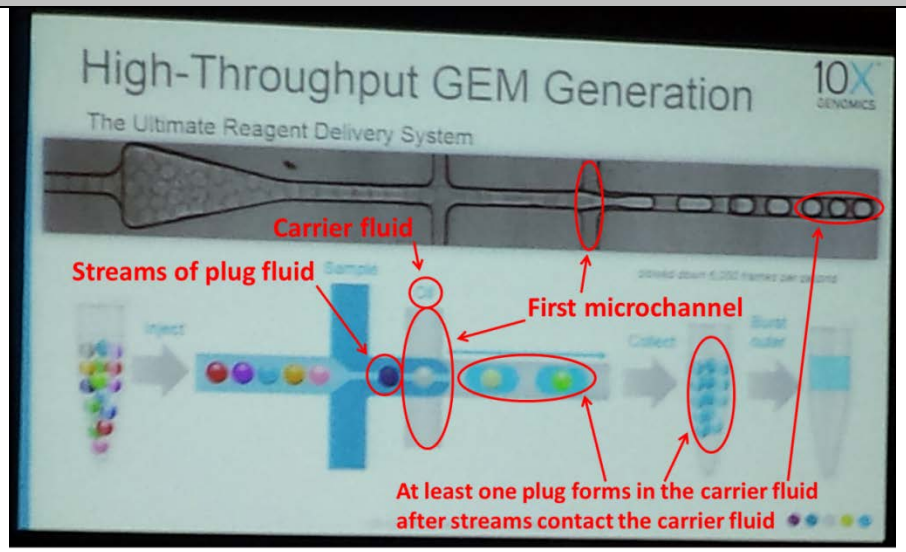
	’091 Claim Language	Infringement Support
		 • The figure below from 10x’s website further notes the introduction of two streams through a central channel. 

	'091 Claim Language	Infringement Support
		Ex. 39 [10X Website Excerpts] at 1. • Similarly, 10X's 2015 JP Morgan presentation shows a microfluidic system through which two streams are introduced to a middle inlet channel.  Ex. 37 [JP Morgan presentation] at 2. • 10X's GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X's product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same "second inlet." This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. A first stream of plug fluid is introduced into

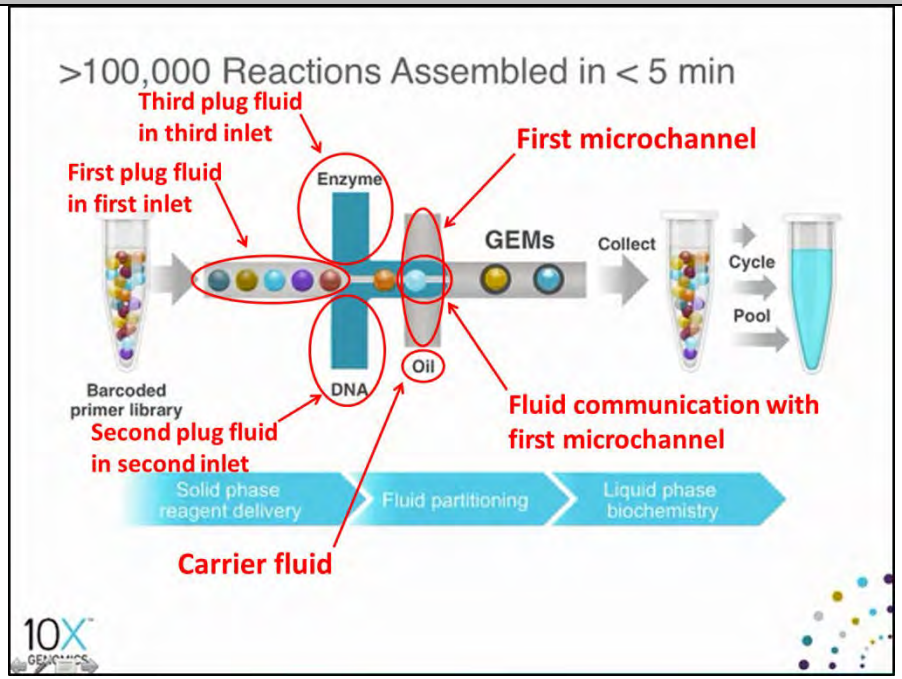
	’091 Claim Language	Infringement Support
		what is labeled as the “first inlet” and a second stream of plug fluid is introduced into the “second inlet.” The first and second streams of plug fluid are in “fluid communication with the first microchannel.”  **The three inlets are in fluid communication with the first channel containing the oil (“carrier-fluid”) such that droplets (“plugs”) form in the oil after the first and second streams of plug fluid contact the oil** • The ’091 patent’s description of “plugs” includes the following: “‘Plugs’ in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible.” Ex. 11 [’091 patent] at 9:20-23.

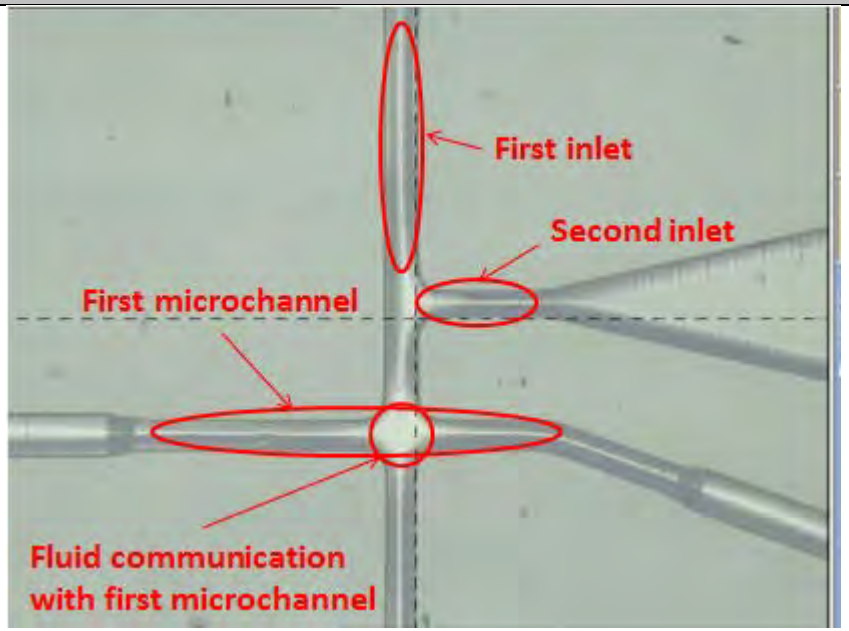
	'091 Claim Language	**Infringement Support**
		• On August 5, 2015, Michael Schnall-Levin, 10X's Vice President of Computational Biology and Applications, presented a webinar "about the GemCode platform." Ex. 4 [10X Webinar] at 3:17-3:23; *see also id.* at 3:35-38 ("I'm really excited today to take you through our Platform."). During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms plugs in the manner described by the '193 patent with reference to the below figure: "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." *Id.* at 9:48-10:39.

	’091 Claim Language	Infringement Support
		 • 10x Technologies’ 2015 presentation at the JP Morgan healthcare conference further shows that plugs are formed after the two inlet streams of plug fluid intersect the oil, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are the light gray circles in the rightmost channel.

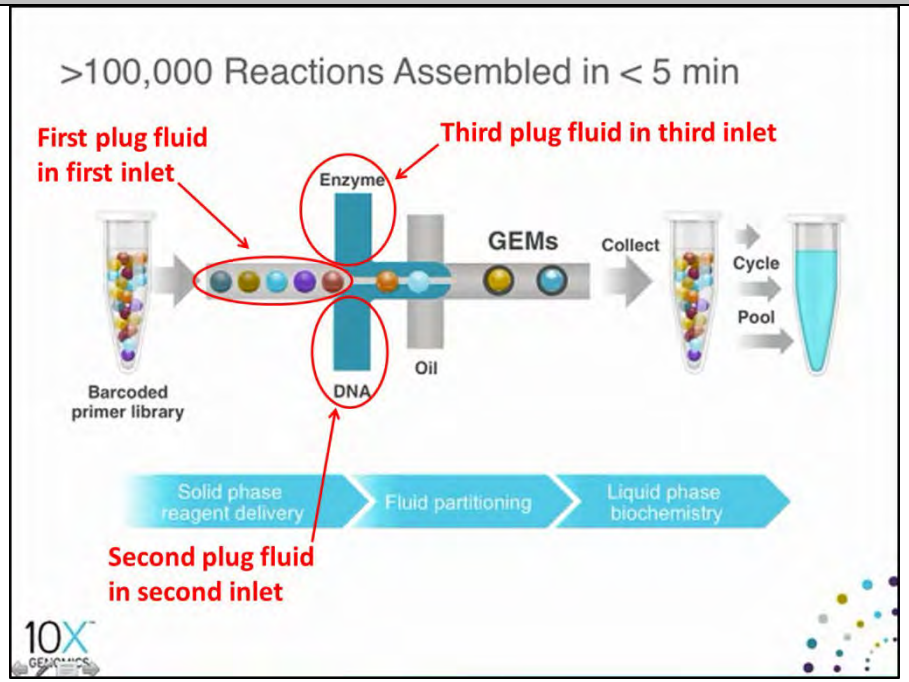
	'091 Claim Language	**Infringement Support**
		 Ex. 37 [JP Morgan presentation] at 2.
091-37d	-a first plug-fluid comprises a first reagent;	10X's GemCode platform has a first plug fluid that comprises a first reagent. • There are at least three streams of plug fluid in 10X's product that each contains one or more reagents: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads, which deliver primers. • The sample DNA is a substrate for a DNA amplification reaction. The enzyme is a reagent that catalyzes the amplification reaction, and is delivered with other reagents (e.g, nucleotides) that are used in the amplification reaction. The gel beads deliver primers that are used in the amplification reaction. • Any one of plug fluids comprising reagents may be designated as the first plug fluid comprising a first reagent. The designations of the first plug fluid, second plug fluid, and third plug fluid in this chart are arbitrary.

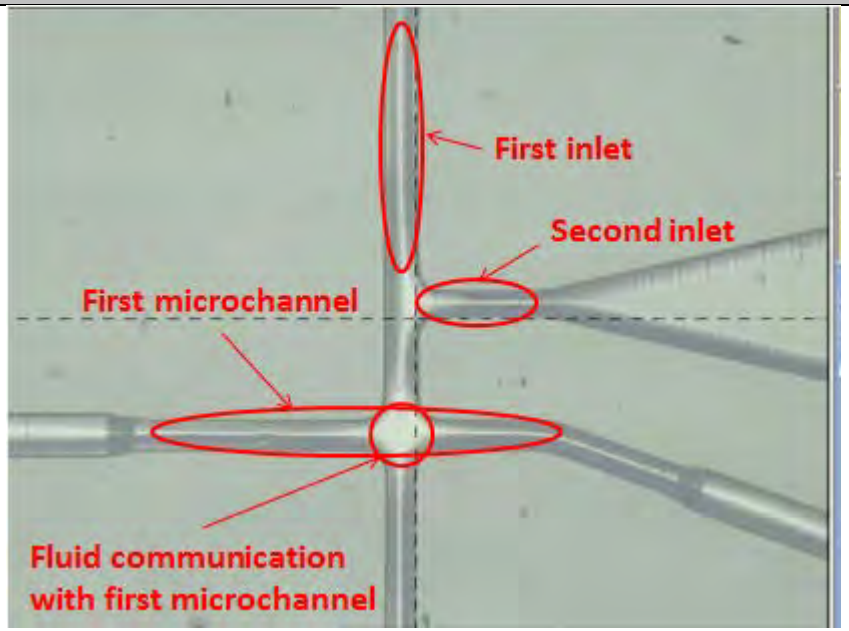
	'091 Claim Language	**Infringement Support**
		10X's GemCode platform has at least three aqueous fluids that each contain one or more reagents. • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is "a cross-section of one of the channels in our microfluidic chip." Ex. 4 [10X Webinar] at 9:33-39. "If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10x. On the second input well the user mixes our biochemical reagents with their DNA.*** And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead." *Id.* at 9:48-10:39.

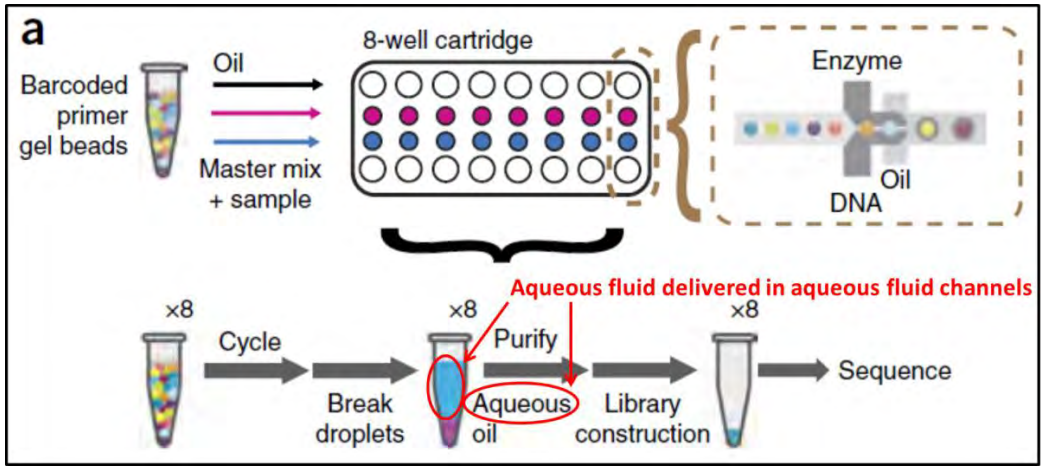
	’091 Claim Language	Infringement Support
		 • 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same “second inlet.” This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. A first stream of plug fluid is introduced into what is labeled as the “first inlet” and is comprised of one or more reagents.

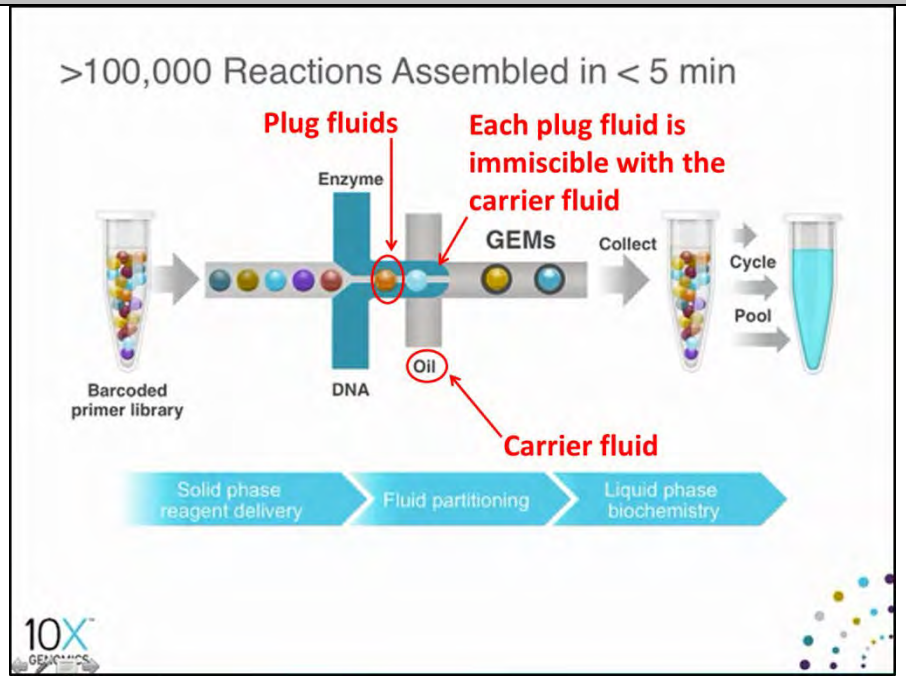
	’091 Claim Language	Infringement Support
		
091-37e	-a second plug-fluid comprises a second reagent;	10X’s GemCode platform has a second plug fluid that comprises a second reagent. • There are at least three streams of plug fluid in 10X’s product that each contains one or more reagents: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads, which deliver primers. • The sample DNA is a substrate for a DNA amplification reaction. The enzyme is a reagent that catalyzes the amplification reaction, and is delivered with other reagents (e.g, nucleotides) that are used in the amplification reaction. The gel beads deliver primers that are used in the amplification reaction. • Any one of plug fluids comprising reagents may be designated as the second plug fluid comprising a second reagent, consistent with the choice that is made for the first plug fluid and reagent. The designations of the first plug fluid, second plug fluid, and third

	'091 Claim Language	**Infringement Support**
		plug fluid in this chart are arbitrary. **<u>10X's GemCode platform has at least three aqueous fluids that each contain one or more reagents.</u>** • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is "a cross-section of one of the channels in our microfluidic chip." Ex. 4 [10X Webinar] at 9:33-39. "If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10x***. ***On the second input well the user mixes our biochemical reagents with their DNA.*** And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead." *Id.* at 9:48-10:39.

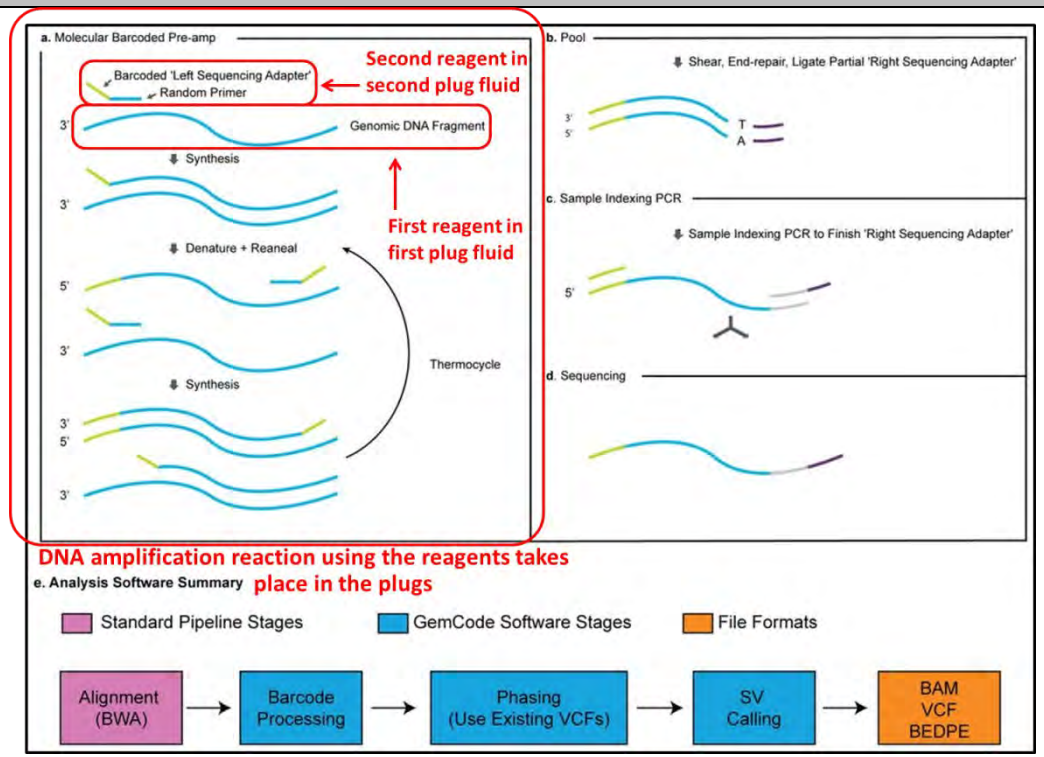
	’091 Claim Language	Infringement Support
		 • 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same “second inlet.” This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. A second stream of plug fluid is introduced into what is labeled as the “second inlet” and is comprised of one or more reagents.

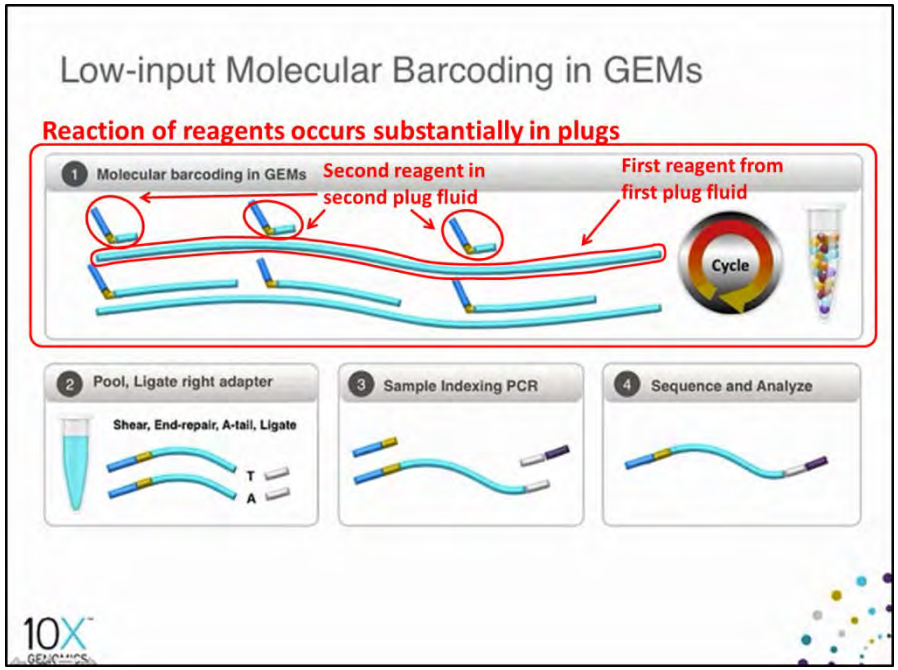
	'091 Claim Language	**Infringement Support**
		
091-37f	-each plug-fluid is immiscible with the carrier-fluid;	**<u>The three plug fluids in 10X's GemCode platform are aqueous and hence immiscible with the oil carrier fluid.</u>** • In 10x's GemCode platform the channels that carry the enzyme, DNA, and barcoded gelbeads for packaging into droplets are aqueous fluid channels. This is shown in 10X's recent *Nature Biotechnology* paper, which describes the operation of 10X's GemCode platform. As explained in this paper, "[t]he first junction combines a close-packed ***aqueous*** slurry of gel beads with the sample and reagent mixture, and the second junction delivers the oil-surfactant solution." Ex. 5 [*Nature Biotechnology*] at 2. The droplets that are formed in 10X's microfluidic device are broken after a DNA amplification reaction is carried out inside the droplet. The fluid that is inside the droplets separates from the oil that originally surrounded and carried the droplets. As

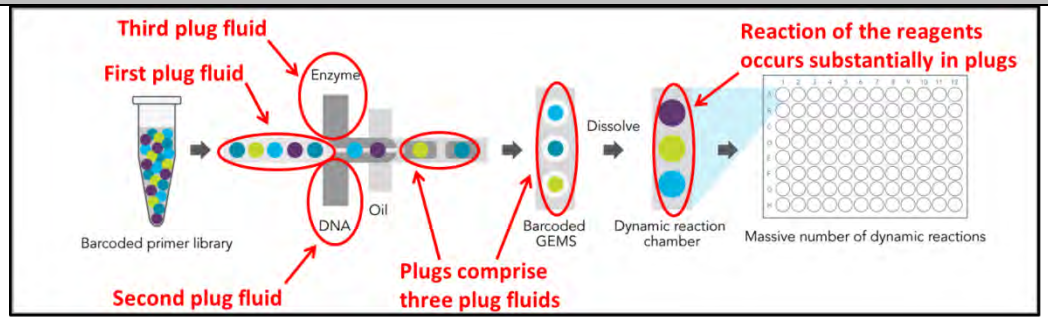
	'091 Claim Language	Infringement Support
		depicted below, the interior of the droplet is "Aqueous" and is shown in blue. Thus, the channels that provided the fluids for the interior of the droplets are aqueous fluid channels.  Ex. 5 [*Nature Biotechnology*] at Fig. 1a. • During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms plugs in the manner described by the '091 patent with reference to the below figure: "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." Ex. 4 [10X Webinar] at 9:48-10:39.

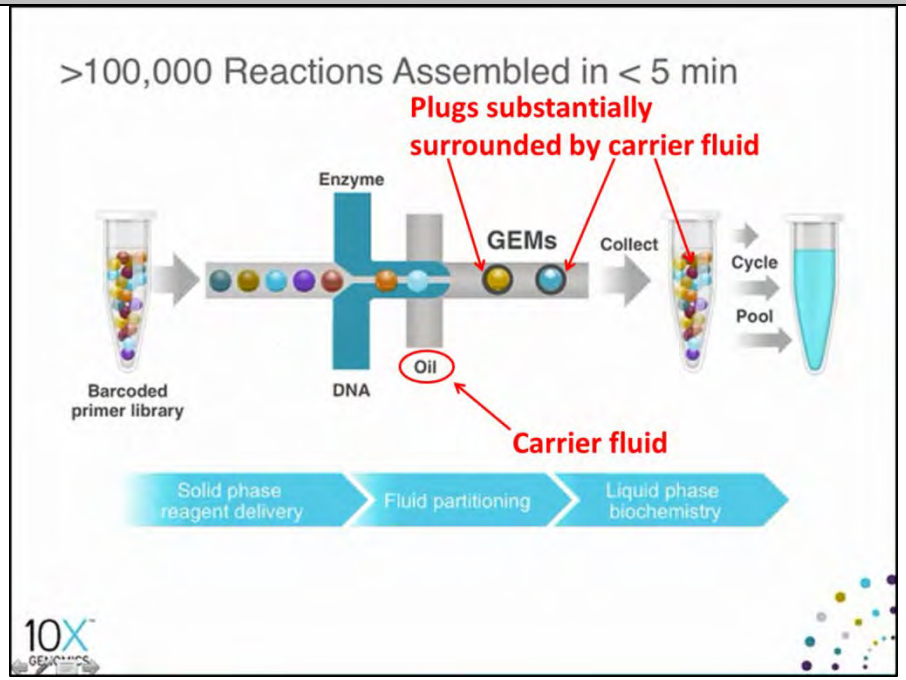
	’091 Claim Language	Infringement Support
		
091-37g	-each plug comprises both the first and second plug-fluids so that the reaction of the reagents substantially occurs in the plug; and	In 10X’s GemCode platform “each plug comprises both the first and second plug-fluids so that the reaction of the reagents substantially occurs in the plug.” • There are at least three streams of plug fluid in 10X’s GemCode platform: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads, which deliver primers. All of these plug fluids are packaged into droplets, and any two of these plug fluids may be selected as the first and second plug fluid. • The reaction that occurs in the droplets using the reagents contained in the plug fluids is a DNA amplification reaction. **The microfluidic droplets (“plugs”) in 10X’s GemCode platform comprise all three of the plug fluids that are used in 10X’s product.**

	'091 Claim Language	**Infringement Support**
		• During his August 2015 presentation, Dr. Schnall-Levin explained that each droplet contains a small portion of the DNA from the user and a gel bead: "If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA.*** And on the third input well the user puts in the oil provided again by 10X. ***There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." Ex. 4 [10X Webinar] at 9:48-10:39. **10X's GemCode platform conducts DNA amplification reactions within the microfluidic droplets ("plugs") using the reagents from the first and second plug fluids** • The reactions which take place within the microfluidic droplets is depicted in the figure below in the panel labeled "a. Molecular Barcoded Pre-amp," which is taken from 10X's recent article in *Nature Biotechnology* that presents data based on the use of 10X's platform. The figure below shows a single stranded "Genomic DNA Fragment" that is extended through the use of a "Random Primer." The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process.

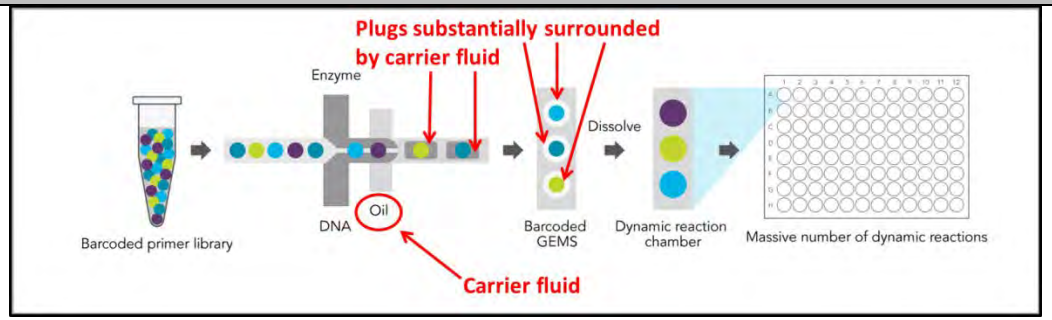
	’091 Claim Language	Infringement Support
		 Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X’s publication states, “1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes.” *Id.* at 3432. • During his August 2015 webinar, Dr. Schall-Levin also described the DNA amplification reaction that takes place in the droplets with reference to the figure below. “So now the biochemistry that’s happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you’ve broken the droplets and put everything back together in bulk. First you can concentrate on the top panel showing the biochemistry

	'091 Claim Language	Infringement Support
		that's happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying.*** The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template." Ex. 4 [10X Webinar] at 13:00-53.  • The figure below from 10x's website depicts the microfluidic system wherein plugs are received in a "dynamic reaction chamber" wherein a "massive number of dynamic reactions" occur.

	’091 Claim Language	Infringement Support
		 Ex. 39 [10X Website Excerpts] at 1.
091-37h	-each plug is substantially surrounded by carrier.	**10X’s GemCode platform forms microfluidic droplets (“plugs”) such that the droplets are substantially surrounded by the oil.** • The ‘091 patent’s description of “plugs” includes the following: “‘Plugs’ in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible.” Ex. 11 [’091 patent] at 9:20-23. • During his August 2015 presentation, Dr. Schnall-Levin described how 10X’s microfluidic device forms plugs in the same manner as the ’091 patent. The process is depicted in the figure below. “If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***.” Ex. 4 [10X Webinar] at 9:48-10:39.

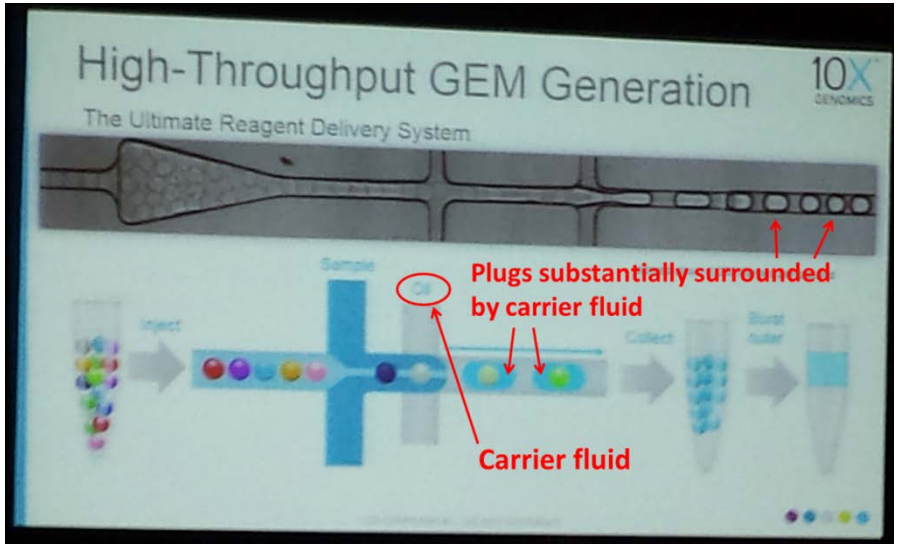
	’091 Claim Language	Infringement Support
		 • As shown in the image above, each microfluidic droplet or plug is called a “GEM” and is substantially surrounded by the grey oil, which is the carrier fluid. • The partitioning of DNA into droplets by 10X’s GemCode system according to the foregoing methods is also established by other resources. For instance, 10x’s website states “The 10X Genomics reagent delivery system randomly partitions DNA fragments, then prepares sequencing libraries in parallel such that all molecules produced within a partition share a unique, partition-specific barcode.” Ex. 39 [10x Website Excerpts] at 1. The website further states that the 10x chip kit “[c]ontains the microfluidic chips and accessories required for ***sample partitioning***.” 10x’s website further shows the formation of the claimed plugs:

	’091 Claim Language	Infringement Support

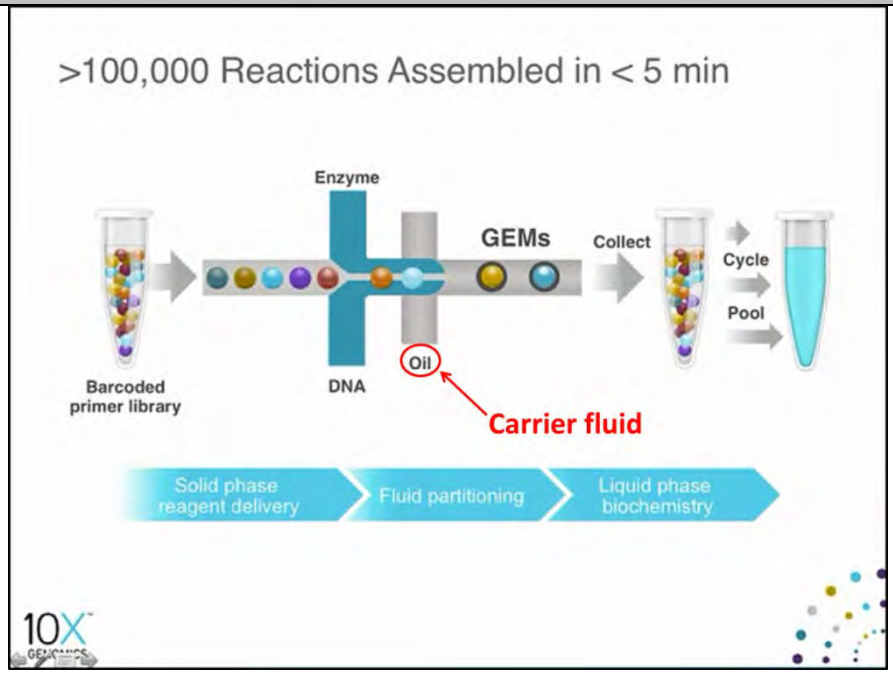
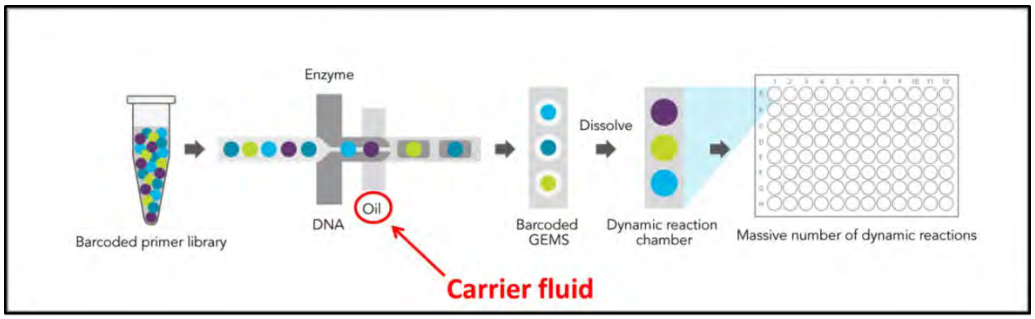


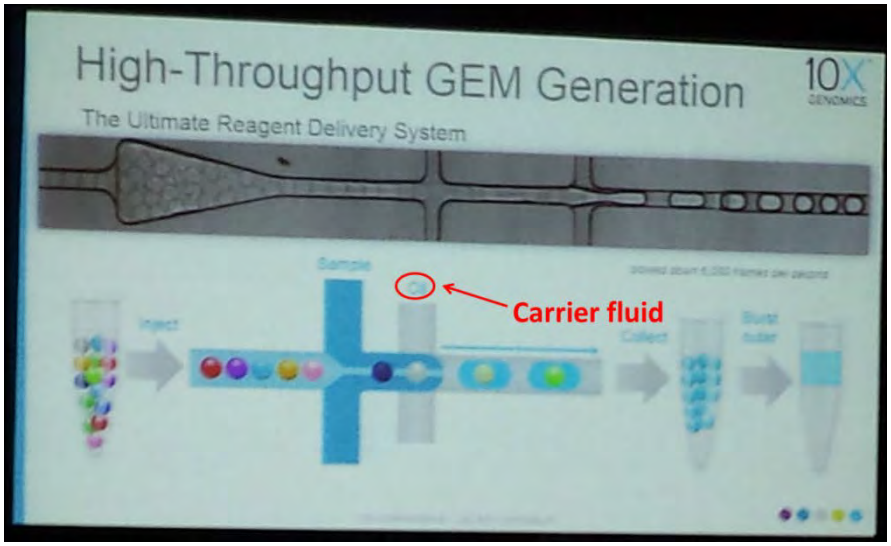
Id. at 1.

- 10x Technologies’ JP Morgan presentation further shows the plugs emerging from the junction of the oil (shown in gray) and the aqueous fluid containing the reagents (shown in blue):

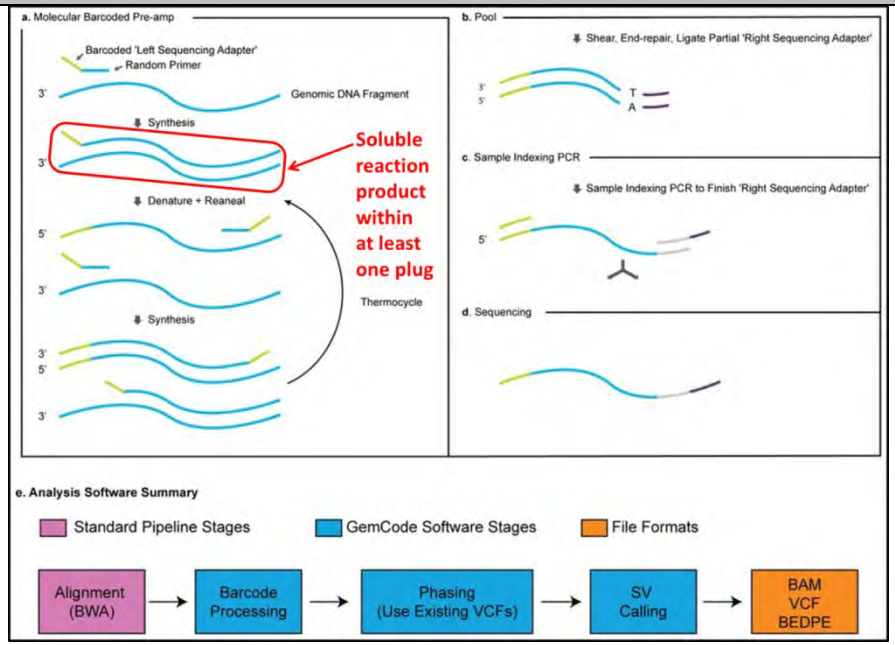


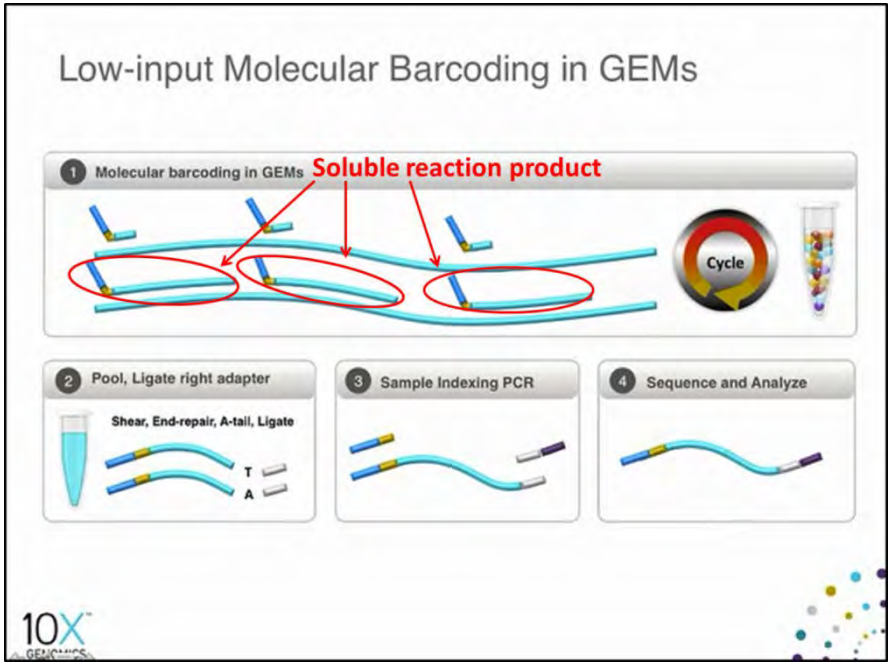
	'091 Claim Language	**Infringement Support**
		Ex. 37 [JP Morgan presentation] at 2.
091-38	38. The method of claim 37, wherein the carrier-fluid comprises an oil.	**<u>The carrier fluid in 10X's GemCode platform is an oil.</u>** • During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms droplets using oil as carrier fluid. The process is depicted in the figure below. "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. ***And on the third input well the user puts in the oil provided again by 10X.*** There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." Ex. 4 [10X Webinar] at 9:48-10:39. Below, two resulting droplets are shown as a yellow and a blue circle. These droplets are encased by the oil, which carries them down the channel for collection.

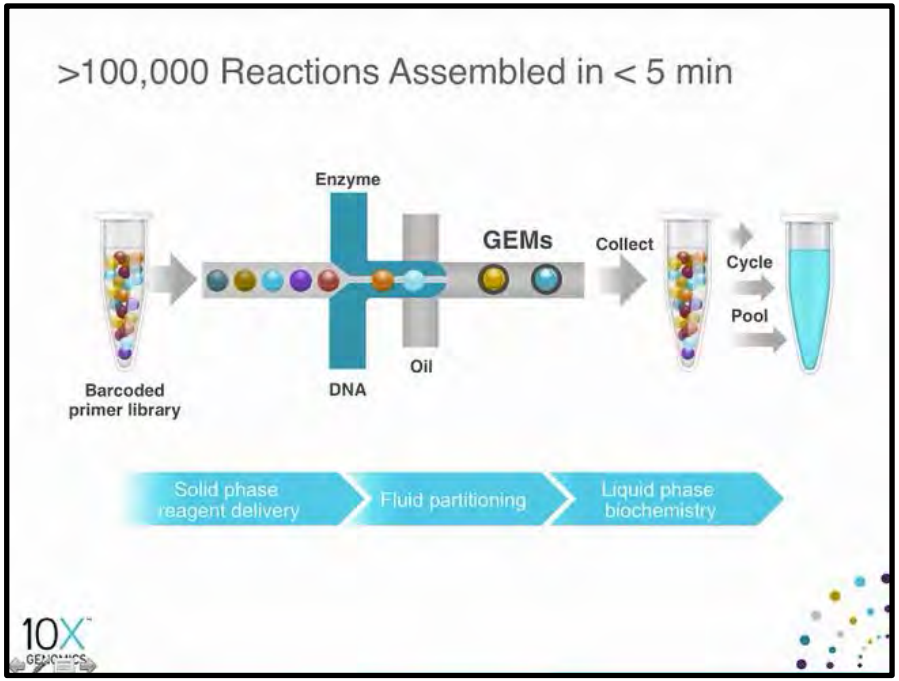
	’091 Claim Language	Infringement Support
		 • 10X’s website further portrays the “oil” carrier fluid (shown in light gray): 

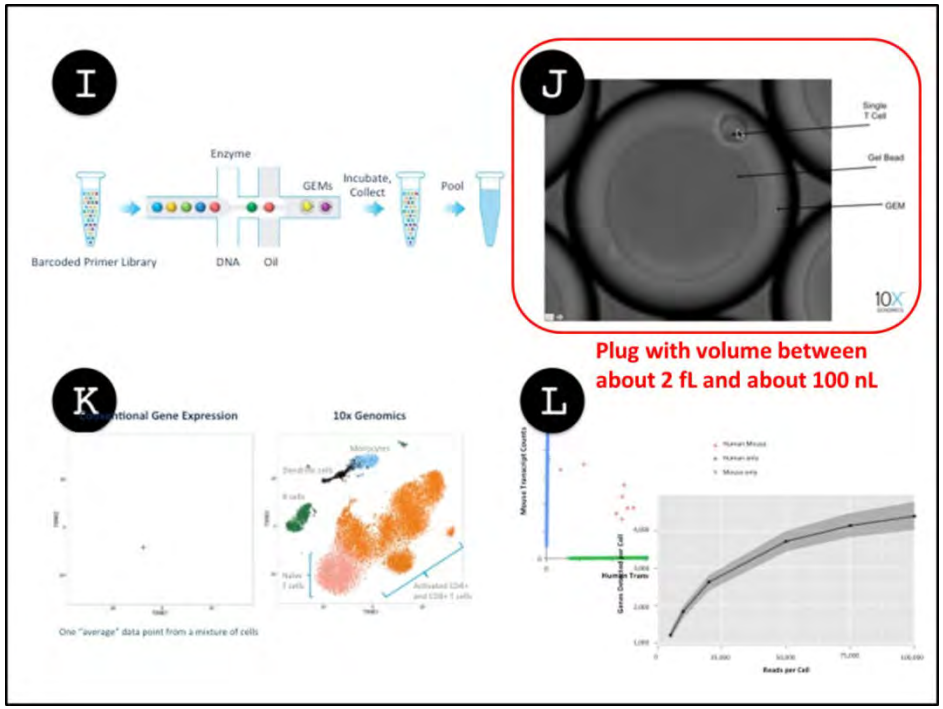
	'091 Claim Language	**Infringement Support**
		Ex. 39 [10X Website Excerpts] at 1. • 10X's 2015 JP Morgan presentation further shows the oil carrier fluid (shown in gray): 
091-39	39. The method of claim 37, wherein the carrier-fluid comprises at least one surfactant.	**<u>The 10X Genomics platform uses oil carrier fluid that comprises a surfactant.</u>** • As 10X describes their system in its recent publication in *Nature Biotechnology*, an "oil-surfactant" solution is used to partition the DNA sample into droplets: "Reagent delivery and sample partitioning are performed in a plastic microfluidic consumable cartridge that processes eight samples simultaneously. Cartridge reservoirs are loaded with gel beads, the sample and reagent mixture and an *oil-surfactant solution*. Reagents are delivered from the reservoirs via a network of microfluidic channels to a microfluidic 'double-cross' junction (Fig. 1a). ***The first junction combines a close-packed aqueous slurry of gel beads with the sample and reagent mixture, and the***

	'091 Claim Language	**Infringement Support**
		second junction delivers the oil-surfactant solution." Ex. 5 [Nature Biotechnology] at 2.
091-43	43. The method of claim 37, wherein the reaction of the plug-fluids forms a soluble reaction product within at least one plug.	**10X's GemCode platform forms a DNA amplification product that is soluble within the aqueous plug fluid.** • The DNA amplification process which occurs in the microfluidic droplets of 10X's GemCode platform is depicted in the figure below in the panel labeled "a. Molecular Barcoded Pre-amp." This figure is taken from 10X's recent article in *Nature Biotechnology*, which presents data based on the use of 10X's GemCode platform. The figure below shows a single stranded "Genomic DNA Fragment" that is extended through the use of a "Random Primer." The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process.

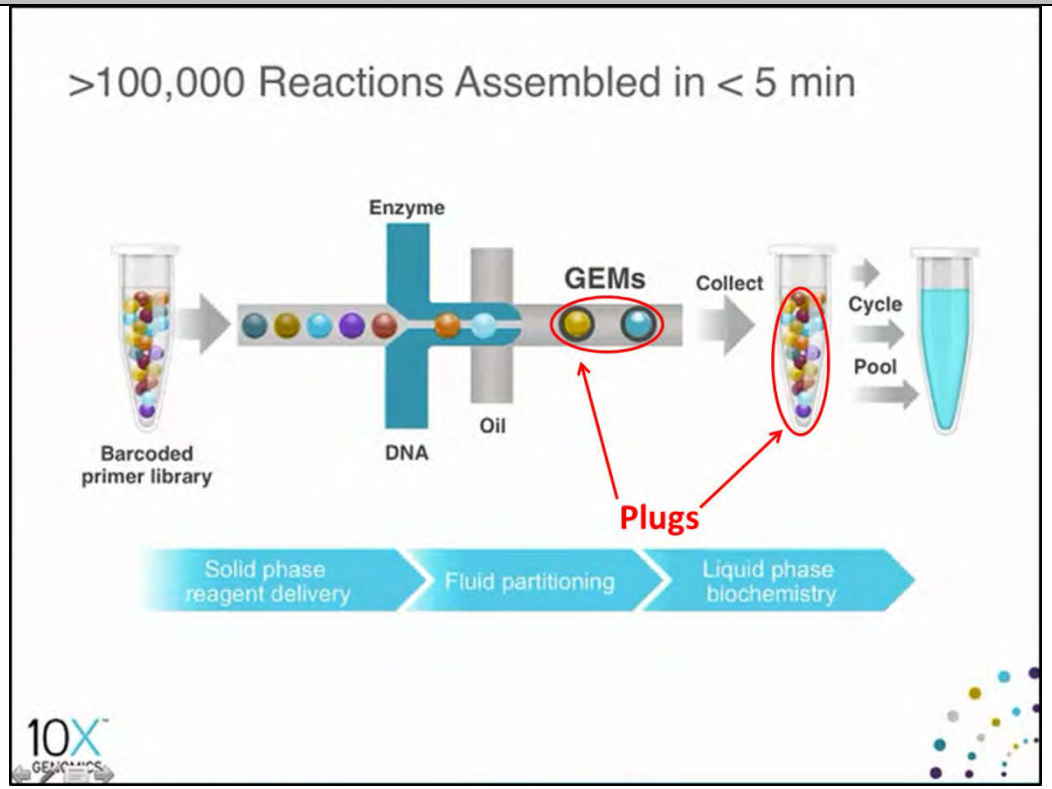
	’091 Claim Language	Infringement Support
		 Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X’s publication states, “1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes.” *Id.* at 3432. The DNA that is formed via the amplification reaction is soluble in water. • During his August 2015 webinar, Dr. Schnall-Levin described the DNA amplification reaction that takes place in the droplets with reference to the figure below. “So now the biochemistry that’s happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you’ve broken the droplets and put everything back together in bulk. First you can concentrate on the top panel showing the biochemistry that’s happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal***

	'091 Claim Language	Infringement Support
		cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying. The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template." Ex. 4 [10X Webinar] at 13:00-53.  • The amplified DNA product is soluble in the aqueous droplets.
091-53	53. The method of claim 37, further comprising employing a number of devices in parallel.	**<u>10X's GemCode platform uses microfluidic chips with eight channels in parallel allowing for eight samples to be tested in parallel.</u>** • As Dr. Schnall Levin explained during his August 2015 webinar, below is a "cross-

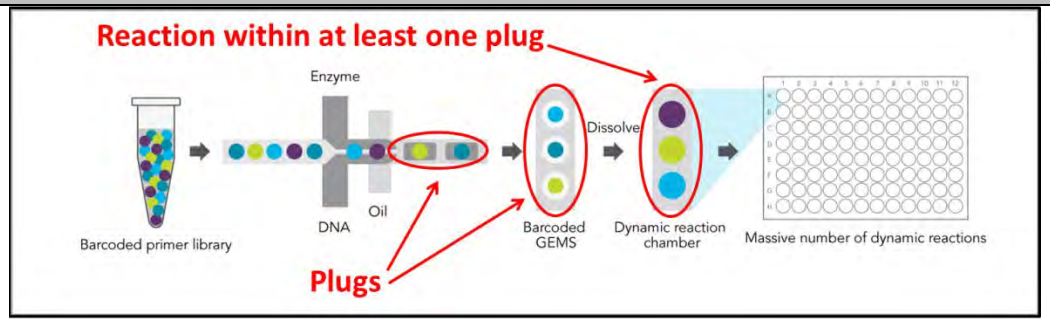
	’091 Claim Language	Infringement Support
		section of one of the channels present in [10X’s] microfluidic chip. ***If you look at one of our microfluidic chips there would be eight of these channels in parallel such that you can run eight samples at a time.***” *Id.* at 9:32-47. 
091-56	56. The method of claim 37, wherein the volume of at least one plug is about 1 femtoliter to about 250 nL.	**<u>10X’s droplets have a volume between 1 femtoliters and about 250 nanoliters</u>**. • At the 2016 AGBT conference, 10X provided a workshop in which it described its technology. The figure below from 10X’s workshop presentation depicts in Panel J a droplet alongside a “Singe T Cell.” Based on the fact that a T cell is roughly 10 µm in

	’091 Claim Language	Infringement Support
		diameter, 10X’s droplets are roughly 100 µm in diameter. This leads to a droplet volume in 10X’s GemCode platform of roughly 0.5 nanoliters, which is between two femtoliters and one hundred nanoliters.  Ex. 41 [Core Genomics] at 4.
091-57a	57. A method of conducting a reaction within at least one plug comprising the steps of:	10X’s GemCode platform uses “method of conducting a reaction within at least one plug.” • The plugs are microfluidic droplets that are formed in 10X’s GemCode platform. • A reaction that is conducted in the plug is a DNA amplification reaction.

	'091 Claim Language	**Infringement Support**
		10X's GemCode platform is a microfluidic system using "plugs," which 10X refers to as droplets or "GEMs". • The '091 patent's description of "plugs" includes the following: "'Plugs' in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible." Ex. 11 ['091 patent] at 9:20-23. • On August 5, 2015, Michael Schnall-Levin, 10X's Vice President of Computational Biology and Applications, presented a webinar "about the GemCode platform." Ex. 4 [10X Webinar] at 3:17-3:23; *see also id.* at 3:35-38 ("I'm really excited today to take you through our Platform."). During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms plugs in the manner described by the '091 patent with reference to the below figure: "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." *Id.* at 9:48-10:39.

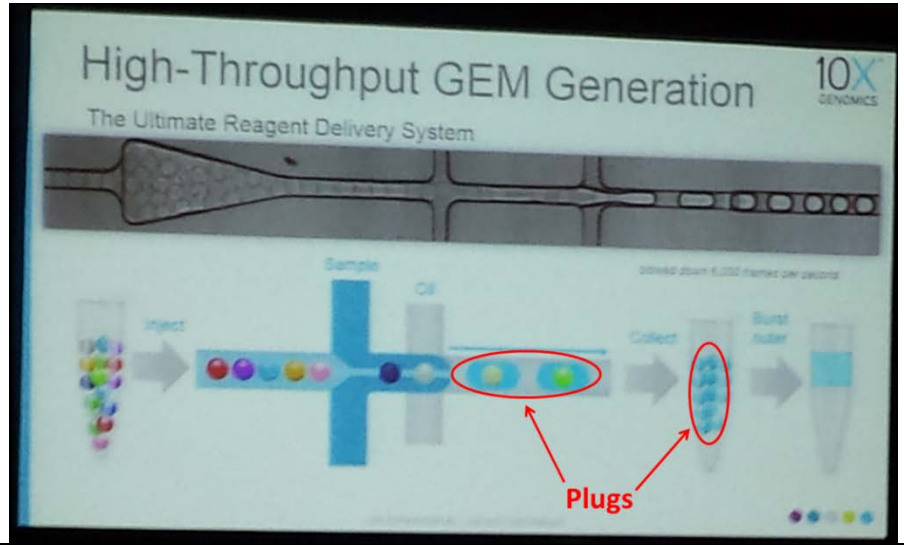
	’091 Claim Language	Infringement Support
		 • 10x’s website is consistent with Dr. Schnall-Levin’s description of 10X’s Platform. 10X’s website states that “[t]he instrument features precise ***microfluidics*** coupled with single button, user-friendly operation.” Ex. 39 [10X Website Excerpts] at 3. The website further states that the 10X chip kit “[c]ontains the ***microfluidic chips*** and accessories required for sample partitioning.” *Id.* at 5.

	’091 Claim Language	Infringement Support

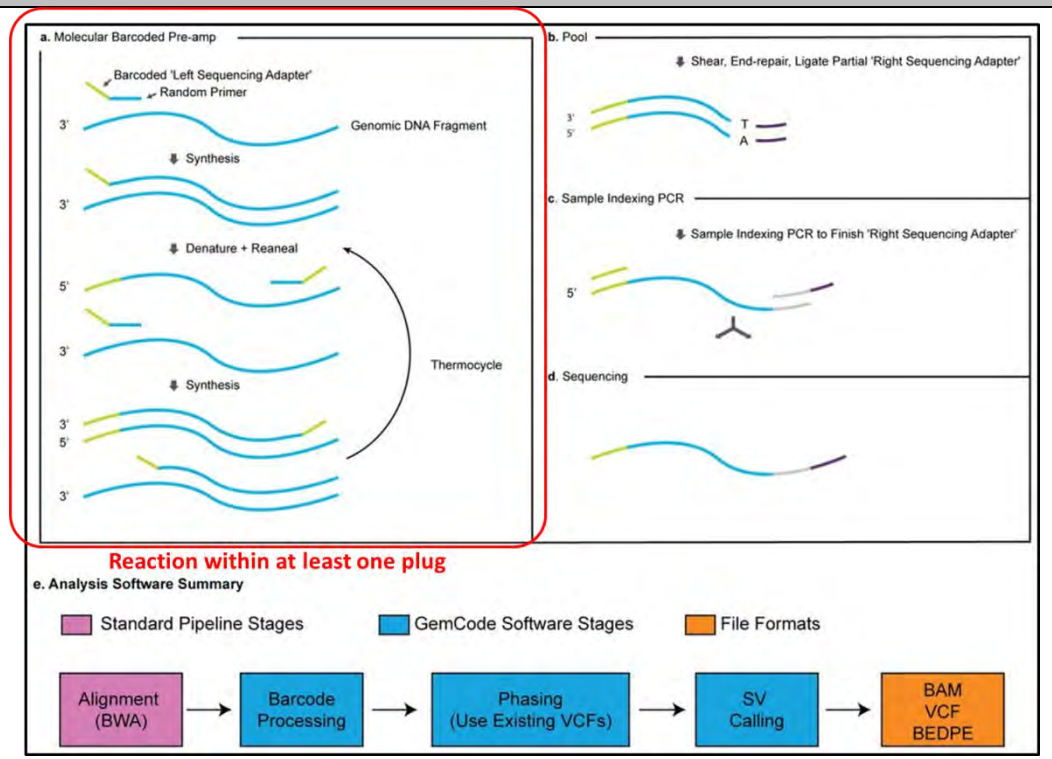


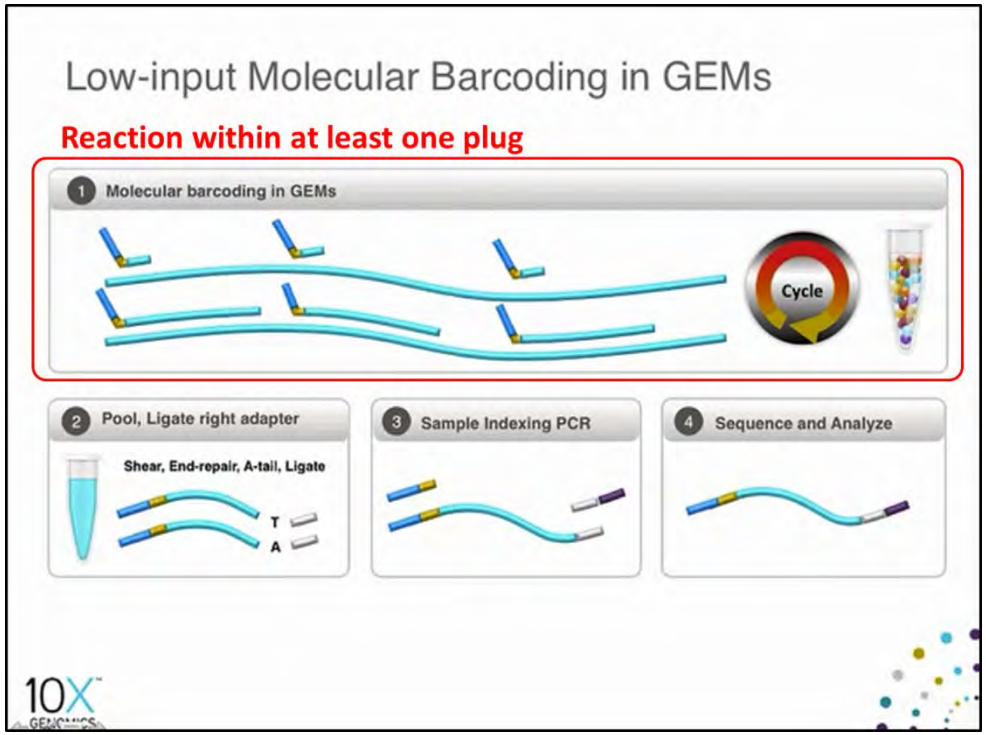
Id. at 1.

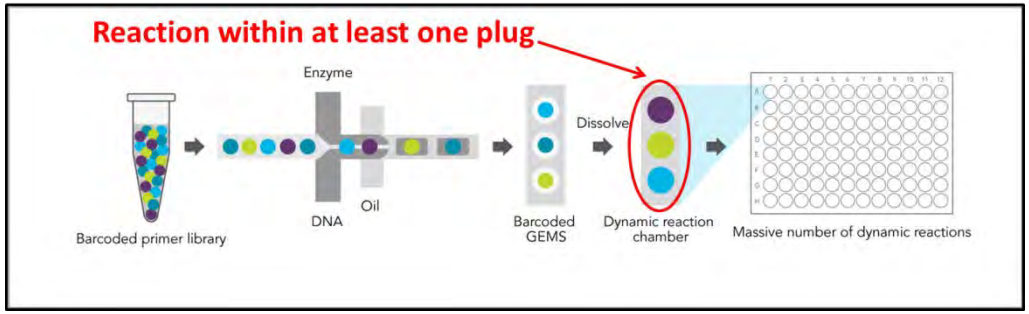
- 10x Technologies’ 2015 presentation at the JP Morgan healthcare conference further shows a microfluidic system for conducting reactions in plugs, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are the light gray circles in the rightmost channel.

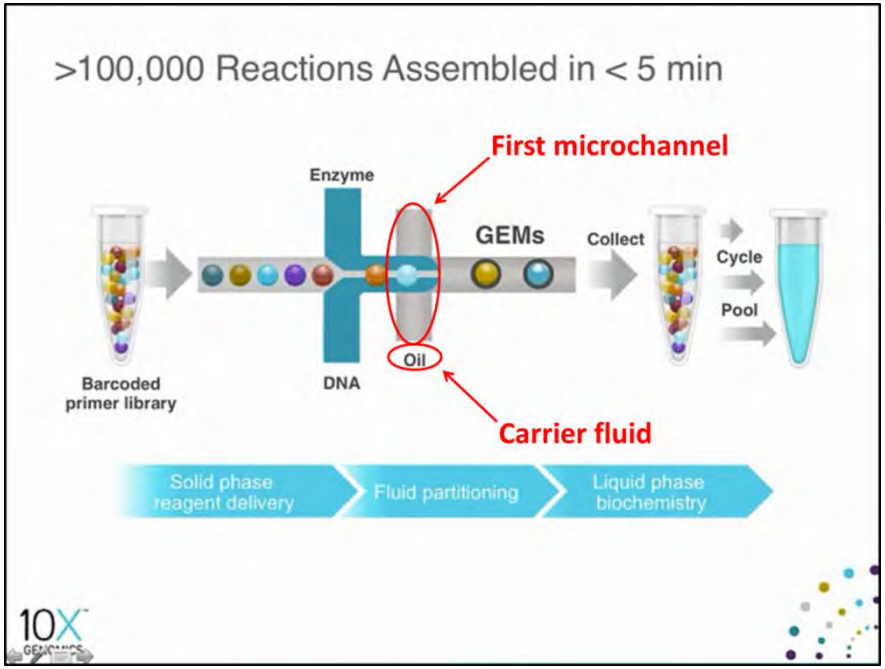


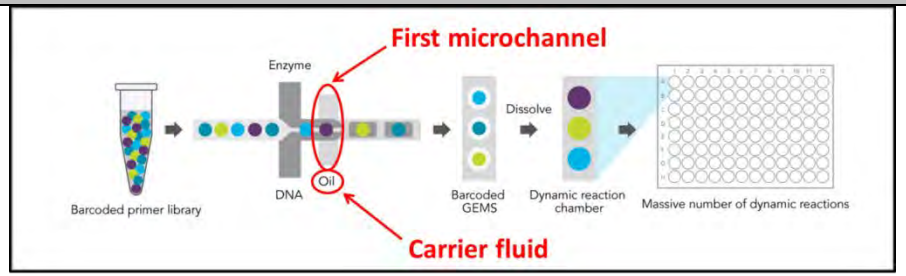
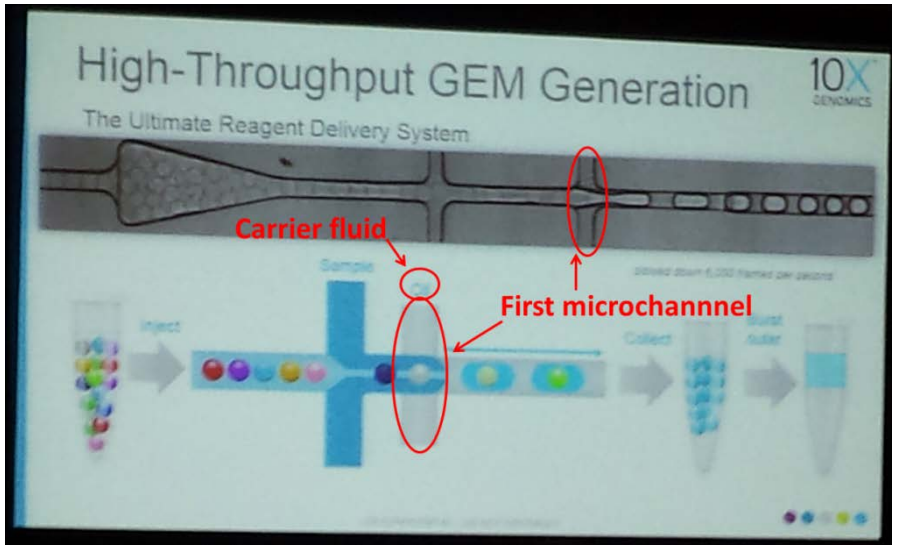
	'091 Claim Language	**Infringement Support**
		Ex. 37 [JP Morgan presentation] at 2. **<u>10X's GemCode platform conducts DNA amplification reactions within the microfluidic droplets ("plugs")</u>** • The slide above from 10X's August 2015 presentation is entitled ">100,000 ***Reactions*** Assembled in <5 min," which demonstrates that reactions are occurring within the microfluidic droplets. • The reactions which take place within the microfluidic droplets is depicted in the figure below in the panel labeled "a. Molecular Barcoded Pre-amp," which is taken from 10X's recent article in *Nature Biotechnology* that presents data based on the use of 10X's platform. The figure below shows a single stranded "Genomic DNA Fragment" that is extended through the use of a "Random Primer." The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process.

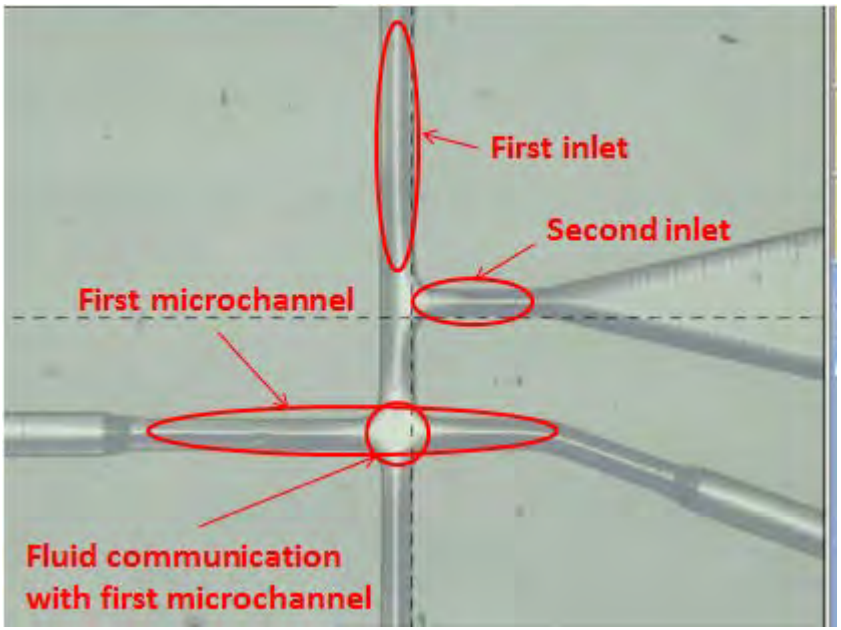
	'091 Claim Language	Infringement Support
		 Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X's publication states, "1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes." *Id.* at 3432. • During his August 2015 webinar, Dr. Schall-Levin also described the DNA amplification reaction that takes place in the droplets with reference to the figure below. "So now the biochemistry that's happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you've broken the droplets and put everything back together in bulk. First you can concentrate on the top panel showing the biochemistry

	'091 Claim Language	Infringement Support
		that's happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying.*** The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template." Ex. 4 [10X Webinar] at 13:00-53.  • The figure below from 10x's website depicts the microfluidic system wherein plugs are received in a "dynamic reaction chamber" wherein a "massive number of dynamic reactions" occur.

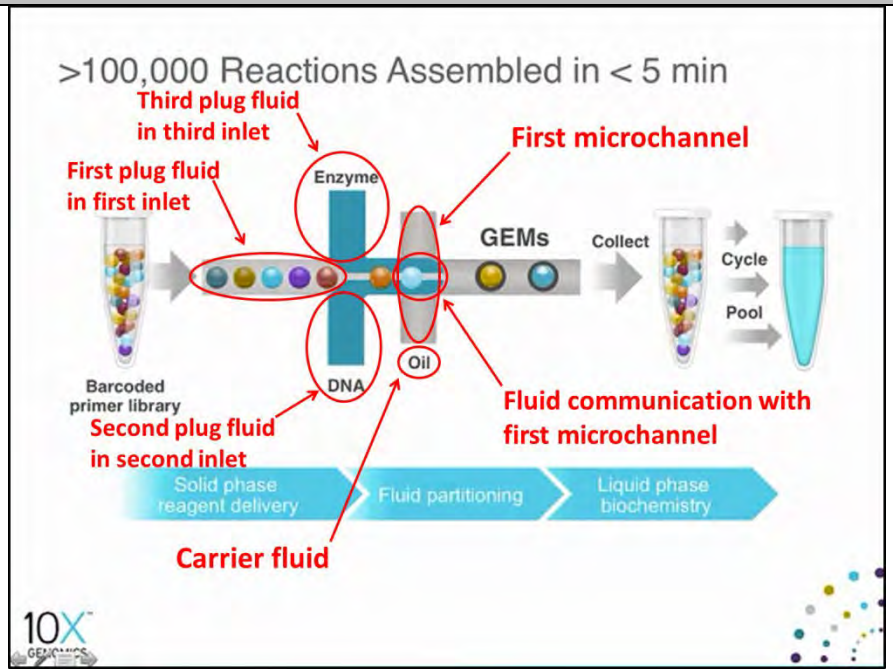
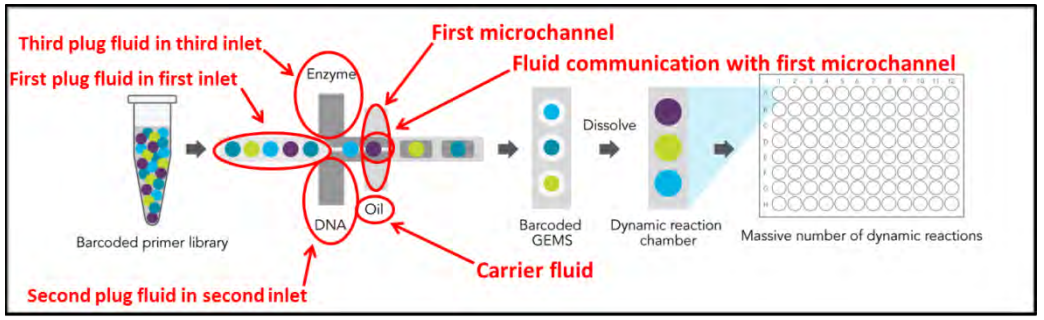
	’091 Claim Language	Infringement Support
		 Ex. 39 [10X Website Excerpts] at 1.
091-57b	introducing a carrier-fluid into a first microchannel of a device;	10X’s GemCode platform introduces “a carrier-fluid into a first microchannel of a device.” • The carrier fluid is the oil that is used in 10X’s microfluidic device. • The first microchannel is the channel through which the stream of oil is introduced perpendicularly into a stream of aqueous fluid that is packaged into droplets. **10X’s GemCode platform introduces an oil (“carrier fluid”) into a first channel of a microfluidic chip.** • During his August webinar, Dr. Schnall-Levin explained that the picture below is “a cross-section of one of the ***channel in our microfluidic chip***.” *Id.* at 9:33-39. “If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And ***on the third input well the user puts in the oil provided again by 10X***. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead.”*** *Id.* at 9:48-10:39. Thus, the channel containing the oil (which is a “carrier fluid immiscible with the aqueous

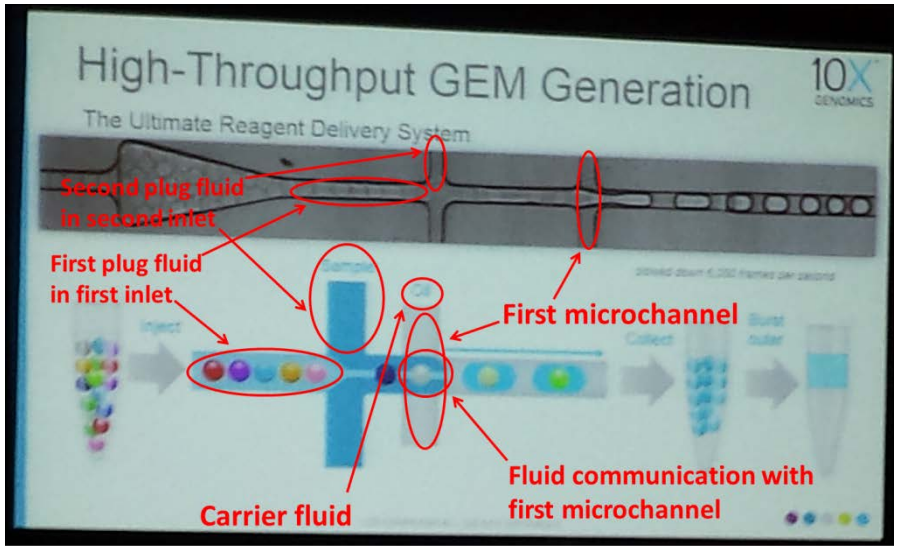
	’091 Claim Language	Infringement Support
		solutions”) intersects and flows into the channel containing the aqueous solution of the gel beads, biochemical reagents and DNA.  • In the figure above the channel containing the continuously flowing oil is shown in grey. • The figure below from 10x’s website further notes the continuously flowing oil from a second channel shown in light grey.

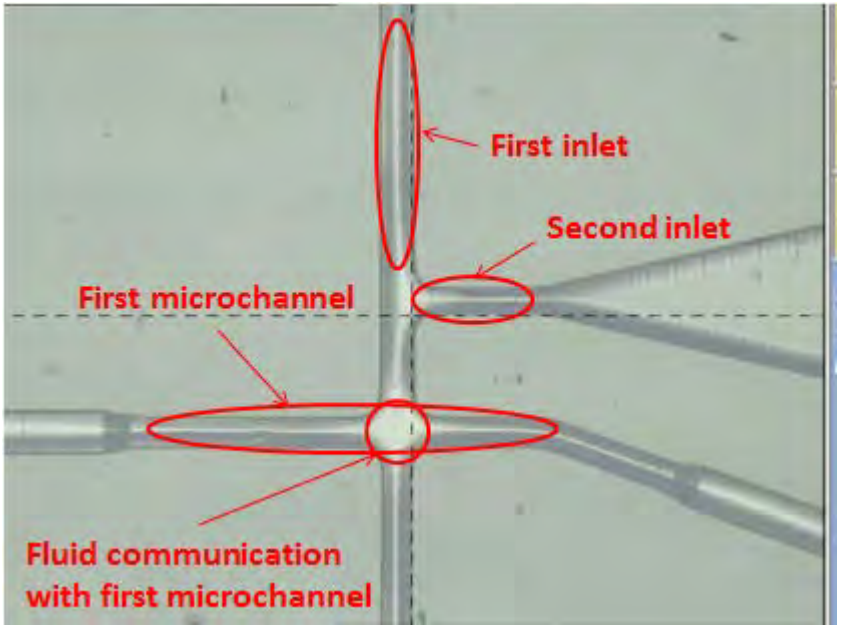
	’091 Claim Language	Infringement Support
		 Ex. 39 [10X Website Excerpts] at 1. • Similarly, 10X’s 2015 JP Morgan presentation shows a microfluidic system through which an oil is shown flowing into a channel of the microfluidic chip in light grey:  Ex. 37 [JP Morgan presentation] at 2.

	’091 Claim Language	Infringement Support
		• 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same inlet. This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. The carrier fluid is introduced into what is labeled “first microchannel.” 
091-57c	introducing a stream of a first plug-fluid into a first	10X’s GemCode platform introduces “a stream of a first plug-fluid into a first inlet in fluid communication with the first microchannel and simultaneously introducing a stream of a

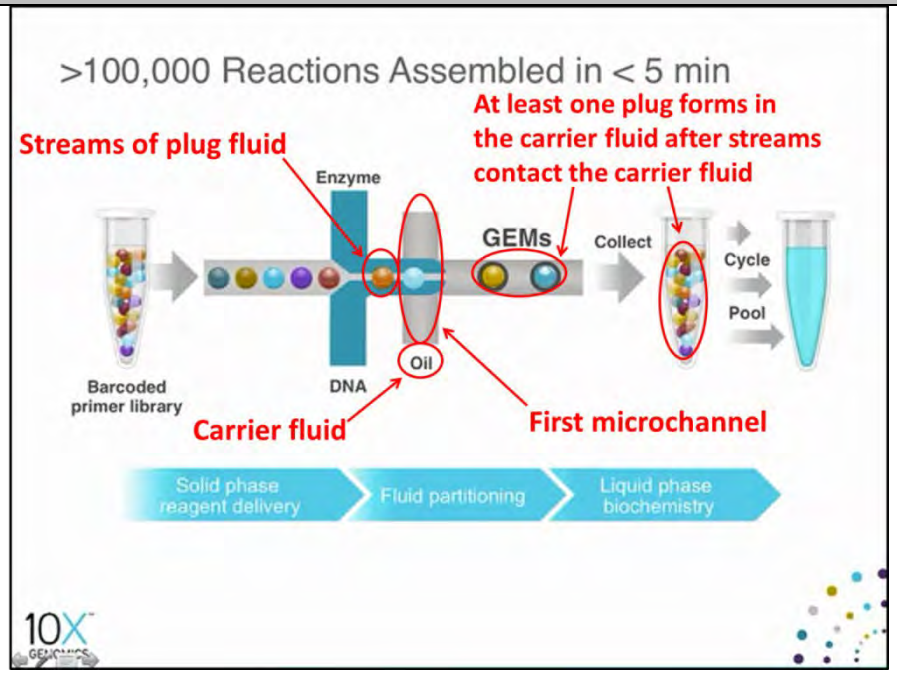
	'091 Claim Language	**Infringement Support**
	inlet in fluid communication with the first microchannel and simultaneously introducing a stream of a second plug-fluid into a second inlet in fluid communication with the first microchannel so that at least one plug forms in the carrier fluid at a junction area of the first and second inlets and the first microchannel; wherein:	second plug-fluid into a second inlet in fluid communication with the first microchannel so that at least one plug forms in the carrier-fluid after the first and second plug-fluids contact The carrier fluid" • There are at least three streams of aqueous fluid in 10X's product: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads. Any two of these fluids may be chosen as the first and second plug fluid. The designations of the first, second, and third fluids in the figures in this chart are arbitrary. • Each of these three plug fluids are introduced via their own inlet. They combine at another inlet that perpendicularly intersects (and is hence in fluid communication with) the first microchannel that carries the oil carrier fluid. • The plugs are the droplets (which 10X sometimes refer to as GEMs) that form at the junction between the inlet and the carrier fluid stream. **10X's GemCode platform simultaneously introduces at least two streams of plug fluid via at least two inlets** • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is "a cross-section of one of the channels in our microfluidic chip." Ex. 4 [10X Webinar] at 9:33-39. "If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads.*** This is a reagent delivered by 10x. ***On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly***. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead." *Id.* at 9:48-10:39. Thus, two streams of plug-fluids, the first containing biochemical reagents and DNA, and the second containing an aqueous solution of the gel beads, are introduced into the same central inlet channel.

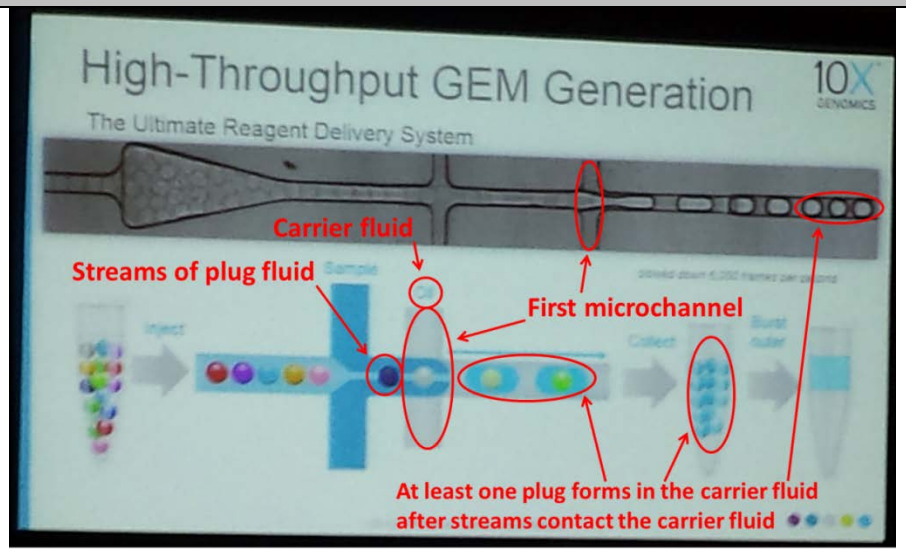
	’091 Claim Language	Infringement Support
		 • The figure below from 10x’s website further notes the introduction of two streams through a central channel. 

	’091 Claim Language	Infringement Support
		Ex. 39 [10X Website Excerpts] at 1. • Similarly, 10X’s 2015 JP Morgan presentation shows a microfluidic system through which two streams are introduced to a middle inlet channel.  Ex. 37 [JP Morgan presentation] at 2. • 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same “second inlet.” This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. A first stream of plug fluid is introduced into

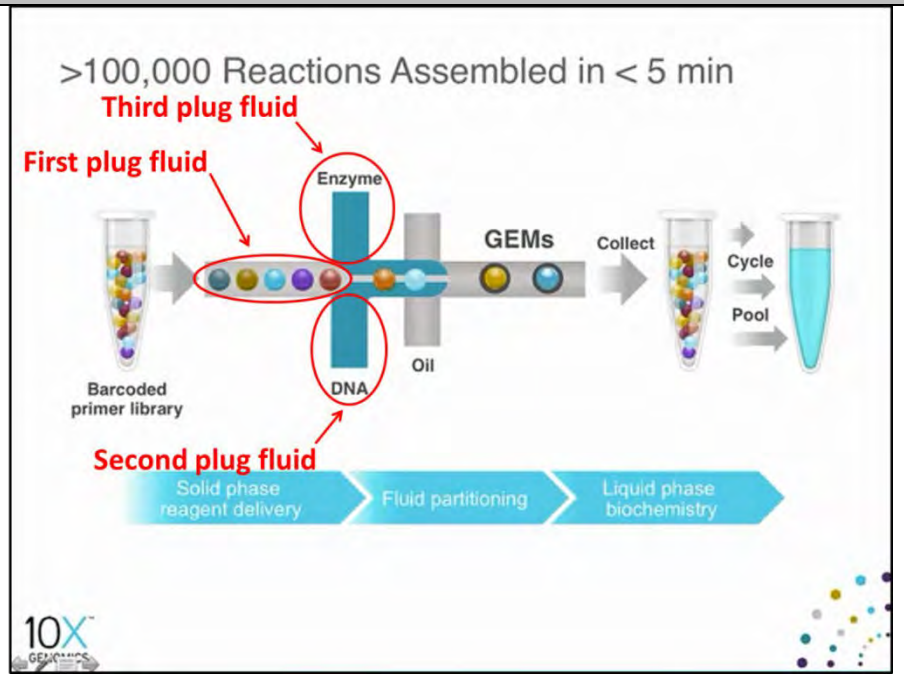
	’091 Claim Language	Infringement Support
		what is labeled as the “first inlet” and a second stream of plug fluid is introduced into the “second inlet.” The first and second streams of plug fluid are in “fluid communication with the first microchannel.”  **The three inlets are in fluid communication with the first channel containing the oil (“carrier-fluid”) such that droplets (“plugs”) form in the oil after the first and second streams of plug fluid contact the oil** • The ’091 patent’s description of “plugs” includes the following: “‘Plugs’ in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible.” Ex. 11 [’091 patent] at 9:20-23.

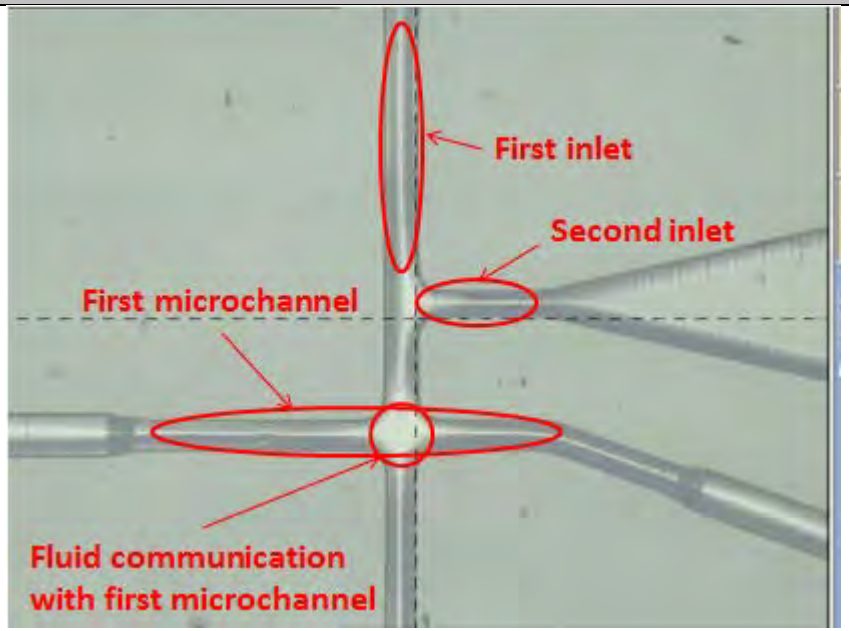
	'091 Claim Language	**Infringement Support**
		• On August 5, 2015, Michael Schnall-Levin, 10X's Vice President of Computational Biology and Applications, presented a webinar "about the GemCode platform." Ex. 4 [10X Webinar] at 3:17-3:23; *see also id.* at 3:35-38 ("I'm really excited today to take you through our Platform."). During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms plugs in the manner described by the '193 patent with reference to the below figure: "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." *Id.* at 9:48-10:39.

	’091 Claim Language	Infringement Support
		 • 10x Technologies’ 2015 presentation at the JP Morgan healthcare conference further shows that plugs are formed after the two inlet streams of plug fluid intersect the oil, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are the light gray circles in the rightmost channel.

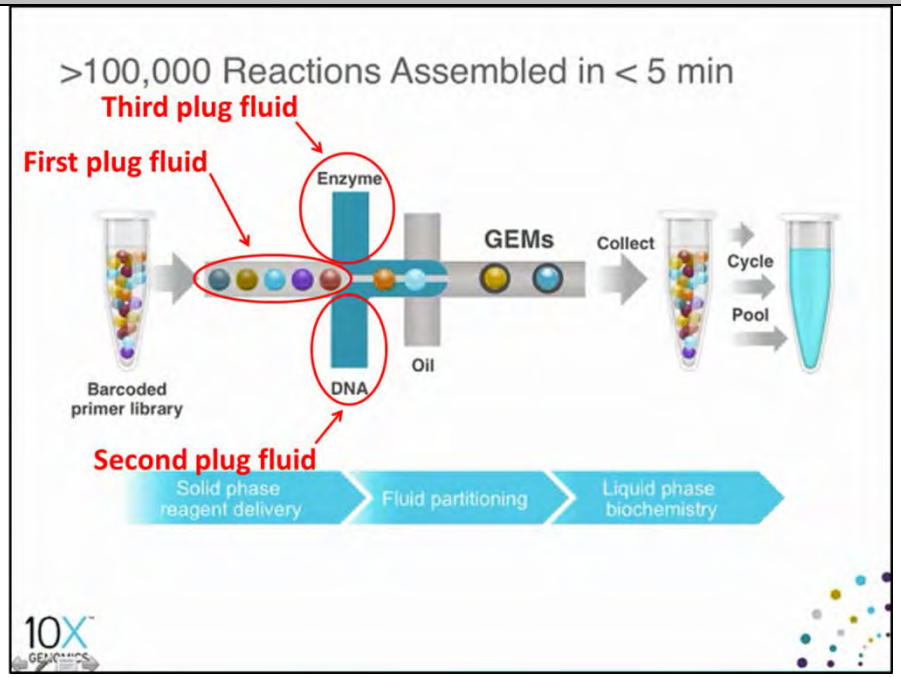
	’091 Claim Language	Infringement Support
		 Ex. 37 [JP Morgan presentation] at 2.
091-57d	-a first plug-fluid comprises a first reagent;	10X’s GemCode platform has a first plug fluid that comprises a first reagent. • There are at least three streams of plug fluid in 10X’s product that each contains one or more reagents: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads, which deliver primers. • The sample DNA is a substrate for a DNA amplification reaction. The enzyme is a reagent that catalyzes the amplification reaction, and is delivered with other reagents (e.g, nucleotides) that are used in the amplification reaction. The gel beads deliver primers that are used in the amplification reaction. • Any one of plug fluids comprising reagents may be designated as the first plug fluid comprising a first reagent. The designations of the first plug fluid, second plug fluid, and third plug fluid in this chart are arbitrary. **10X’s GemCode platform has at least three aqueous fluids that each contain one or more**

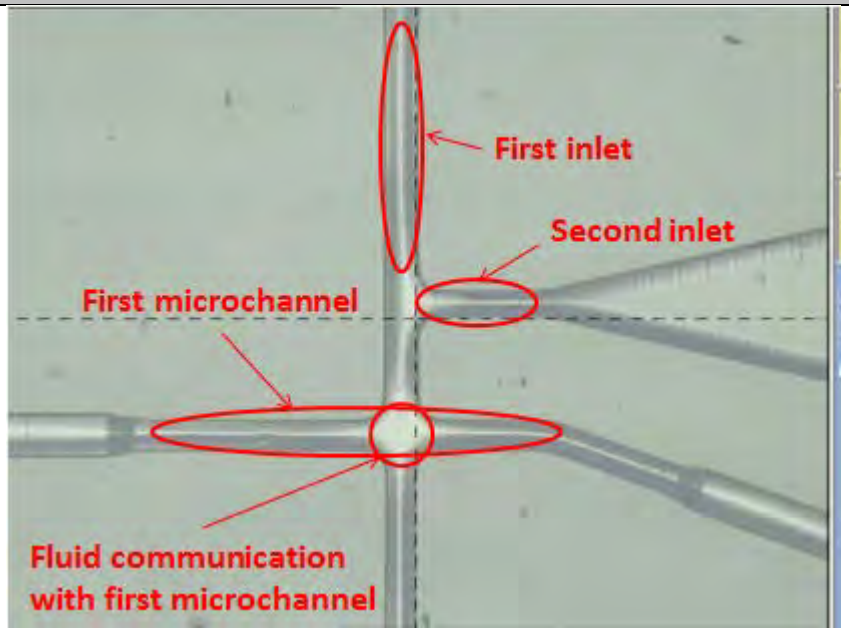
	'091 Claim Language	**Infringement Support**
		reagents. • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is "a cross-section of one of the channels in our microfluidic chip." Ex. 4 [10X Webinar] at 9:33-39. "If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10x. On the second input well the user mixes our biochemical reagents with their DNA.*** And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead." *Id.* at 9:48-10:39.

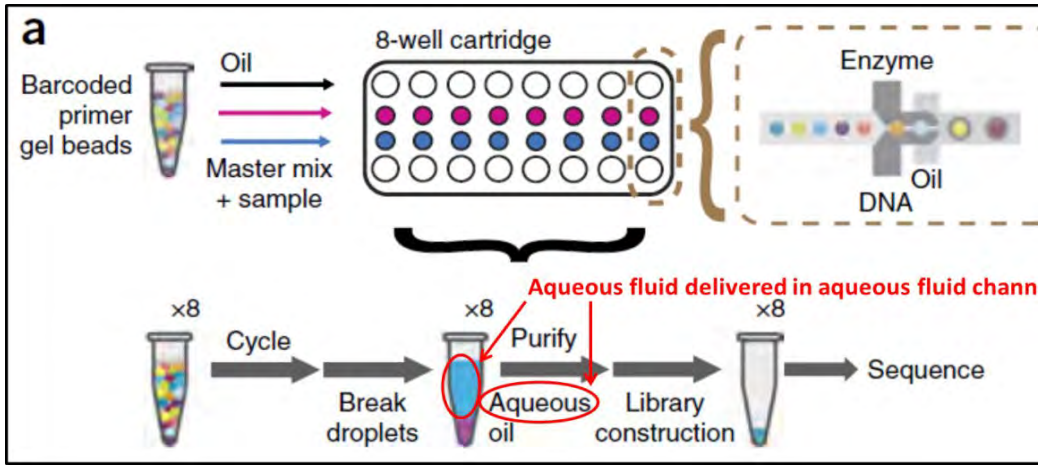
	’091 Claim Language	Infringement Support
		 • 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same “second inlet.” This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. A first stream of plug fluid is introduced into what is labeled as the “first inlet” and is comprised of one or more reagents.

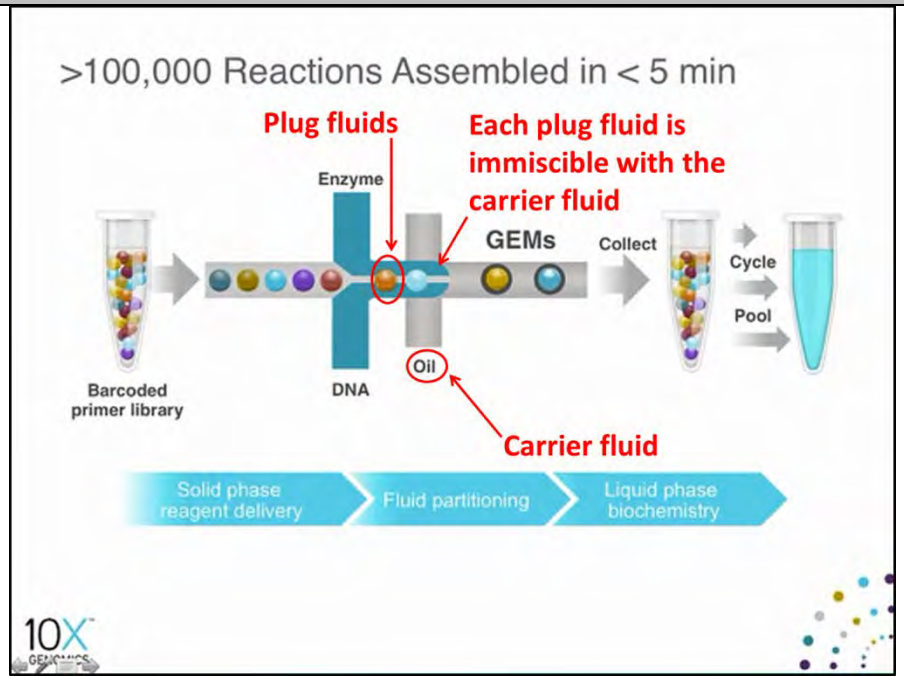
	'091 Claim Language	**Infringement Support**
		
091-57e	-a second plug-fluid comprises a second reagent;	10X's GemCode platform has a second plug fluid that comprises a second reagent. • There are at least three streams of plug fluid in 10X's product that each contains one or more reagents: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads, which deliver primers. • The sample DNA is a substrate for a DNA amplification reaction. The enzyme is a reagent that catalyzes the amplification reaction, and is delivered with other reagents (e.g, nucleotides) that are used in the amplification reaction. The gel beads deliver primers that are used in the amplification reaction. • Any one of plug fluids comprising reagents may be designated as the second plug fluid comprising a second reagent, consistent with the choice that is made for the first plug fluid and reagent. The designations of the first plug fluid, second plug fluid, and third

	'091 Claim Language	**Infringement Support**
		plug fluid in this chart are arbitrary. **<u>10X's GemCode platform has at least three aqueous fluids that each contain one or more reagents.</u>** • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is "a cross-section of one of the channels in our microfluidic chip." Ex. 4 [10X Webinar] at 9:33-39. "If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10x***. ***On the second input well the user mixes our biochemical reagents with their DNA.*** And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead." *Id.* at 9:48-10:39.

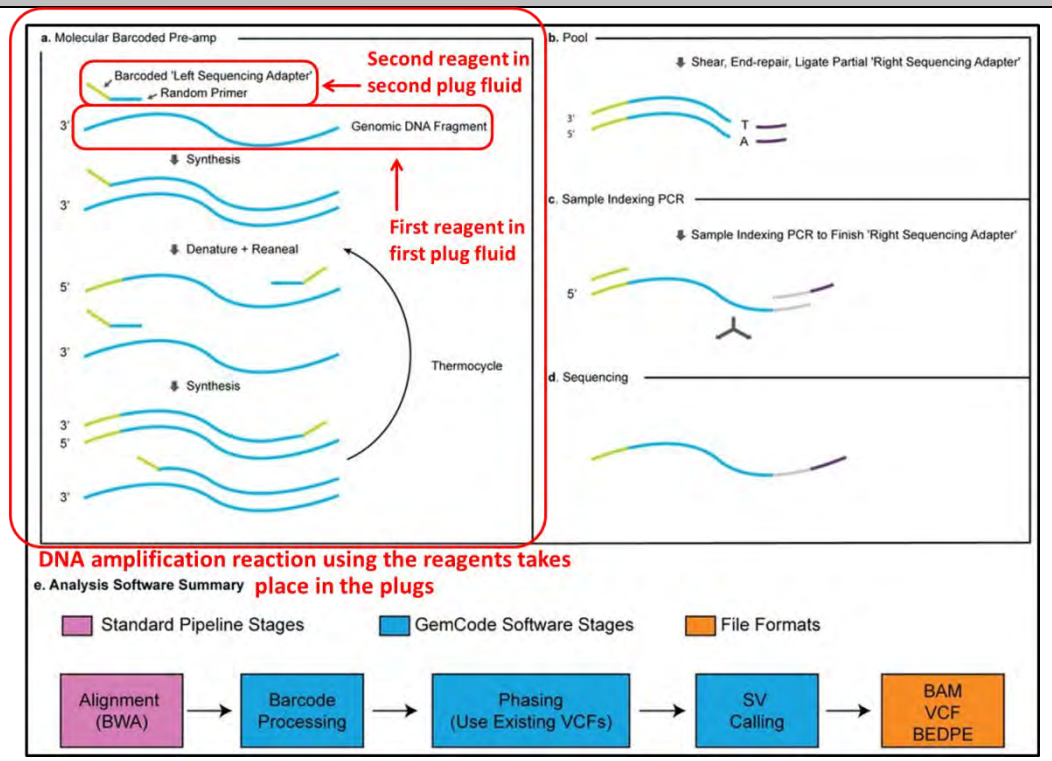
	'091 Claim Language	Infringement Support
		 • 10X's GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X's product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same "second inlet." This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. A second stream of plug fluid is introduced into what is labeled as the "second inlet" and is comprised of one or more reagents.

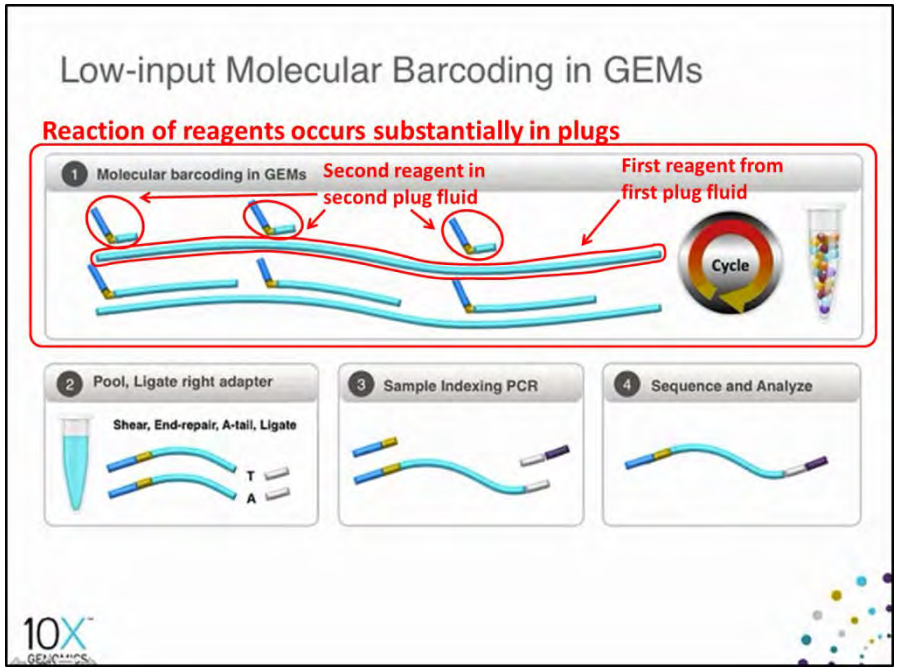
	'091 Claim Language	**Infringement Support**
		
091-57f	-each plug-fluid is immiscible with the carrier-fluid;	**The three plug fluids in 10X's GemCode platform are aqueous and hence immiscible with the oil carrier fluid.** • In 10x's GemCode platform the channels that carry the enzyme, DNA, and barcoded gelbeads for packaging into droplets are aqueous fluid channels. This is shown in 10X's recent *Nature Biotechnology* paper, which describes the operation of 10X's GemCode platform. As explained in this paper, "[t]he first junction combines a close-packed ***aqueous*** slurry of gel beads with the sample and reagent mixture, and the second junction delivers the oil-surfactant solution." Ex. 5 [*Nature Biotechnology*] at 2. The droplets that are formed in 10X's microfluidic device are broken after a DNA amplification reaction is carried out inside the droplet. The fluid that is inside the droplets separates from the oil that originally surrounded and carried the droplets. As depicted below, the interior of the droplet is "Aqueous" and is shown in blue. Thus,

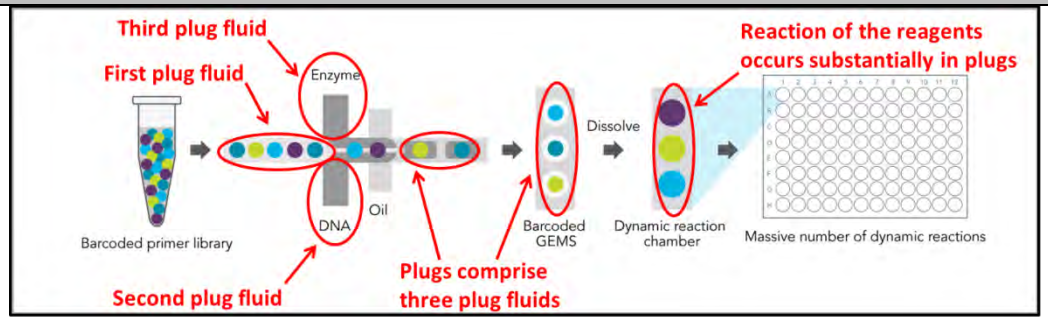
	’091 Claim Language	Infringement Support
		the channels that provided the fluids for the interior of the droplets are aqueous fluid channels.  Ex. 5 [*Nature Biotechnology*] at Fig. 1a. • During his August 2015 presentation, Dr. Schnall-Levin described how 10X’s microfluidic device forms plugs in the manner described by the ‘091 patent with reference to the below figure: “If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***.” Ex. 4 [10X Webinar] at 9:48-10:39.

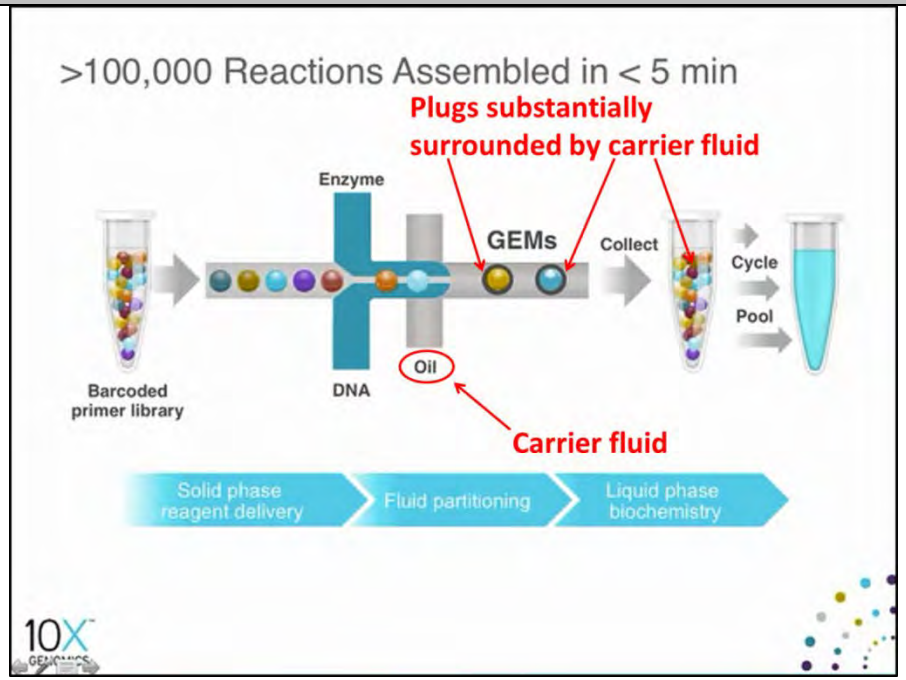
	’091 Claim Language	Infringement Support
		 • As shown in the above image, the blue fluid and colored gel beads are immiscible with the oil because the intersection forms isolated droplets rather than a homogenous liquid.
091-57g	-each plug comprises both the first and second plug-fluids so that the reaction of the reagents substantially occurs in the plug; and	In 10X’s GemCode platform “each plug comprises both the first and second plug-fluids so that the reaction of the reagents substantially occurs in the plug.” • There are at least three streams of plug fluid in 10X’s GemCode platform: (1) the aqueous fluid containing the sample DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads, which deliver primers. All of these plug fluids are packaged into droplets, and any two of these plug fluids may be selected as the first and second plug fluid. • The reaction that occurs in the droplets using the reagents contained in the plug fluids

	’091 Claim Language	Infringement Support
		is a DNA amplification reaction. **<u>The microfluidic droplets (“plugs”) in 10X’s GemCode platform comprise all three of the plug fluids that are used in 10X’s product.</u>** • During his August 2015 presentation, Dr. Schnall-Levin explained that each droplet contains a small portion of the DNA from the user and a gel bead: “If you look starting from left to right what you see is the channels that are from three different input wells. ***On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA.*** And on the third input well the user puts in the oil provided again by 10X. ***There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***.” Ex. 4 [10X Webinar] at 9:48-10:39. **<u>10X’s GemCode platform conducts DNA amplification reactions within the microfluidic droplets (“plugs”) using the reagents from the first and second plug fluids</u>** • The reactions which take place within the microfluidic droplets is depicted in the figure below in the panel labeled “a. Molecular Barcoded Pre-amp,” which is taken from 10X’s recent article in *Nature Biotechnology* that presents data based on the use of 10X’s platform. The figure below shows a single stranded “Genomic DNA Fragment” that is extended through the use of a “Random Primer.” The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process.

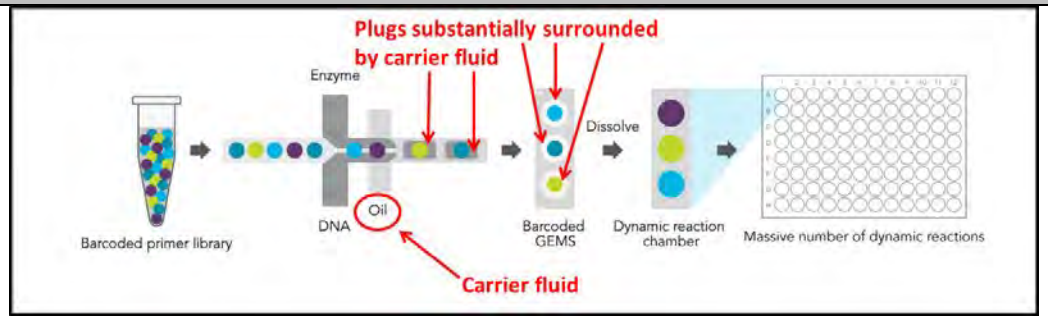
	'091 Claim Language	Infringement Support
		 Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X's publication states, "1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes." *Id.* at 3432. • During his August 2015 webinar, Dr. Schall-Levin also described the DNA amplification reaction that takes place in the droplets with reference to the figure below. "So now the biochemistry that's happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you've broken the droplets and put everything back together in bulk. First you can concentrate on the top panel showing the biochemistry

	'091 Claim Language	Infringement Support
		that's happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying.*** The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template." Ex. 4 [10X Webinar] at 13:00-53.  • The figure below from 10x's website depicts the microfluidic system wherein plugs are received in a "dynamic reaction chamber" wherein a "massive number of dynamic reactions" occur.

	’091 Claim Language	Infringement Support
		 Ex. 4 [10X Webinar] at 1.
091-57h	-each plug is substantially surrounded by carrier.	**10X’s GemCode platform forms microfluidic droplets (“plugs”) such that the droplets are substantially surrounded by the oil.** • The ‘091 patent’s description of “plugs” includes the following: “’Plugs’ in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible.” Ex. 11 [’091 patent] at 9:20-23. • During his August 2015 presentation, Dr. Schnall-Levin described how 10X’s microfluidic device forms plugs in the same manner as the ’091 patent. The process is depicted in the figure below. “If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***.” Ex. 4 [Webinar] at 9:48-10:39.

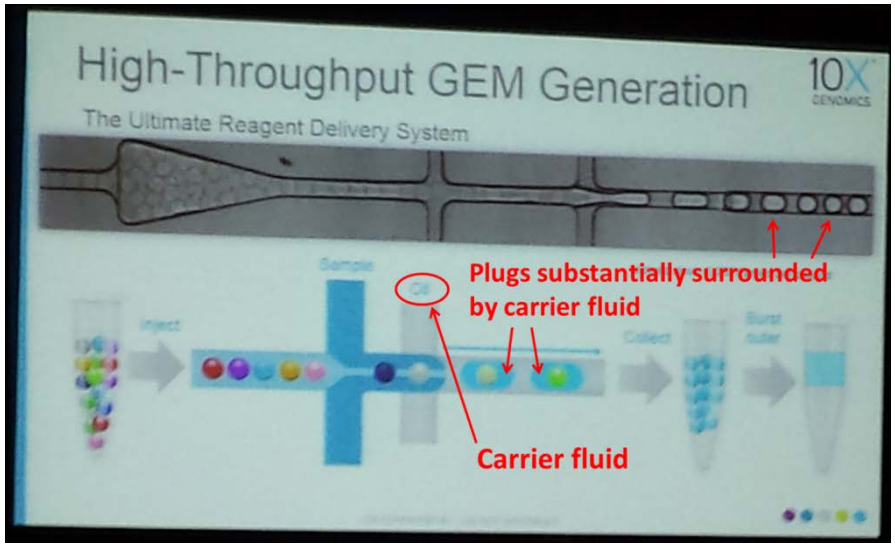
	'091 Claim Language	Infringement Support
		 • As shown in the image above, each microfluidic droplet or plug is called a "GEM" and is substantially surrounded by the grey oil, which is the carrier fluid. The partitioning of DNA into droplets by 10X's GemCode system according to the foregoing methods is also established by other resources. For instance, 10x's website states "The 10X Genomics reagent delivery system randomly partitions DNA fragments, then prepares sequencing libraries in parallel such that all molecules produced within a partition share a unique, partition-specific barcode." Ex. 39 [10x Website Excerpts] at 1. The website further states that the 10x chip kit "[c]ontains the microfluidic chips and accessories required for ***sample partitioning***." *Id.* at 5. 10x's website further shows the formation of the claimed plugs:

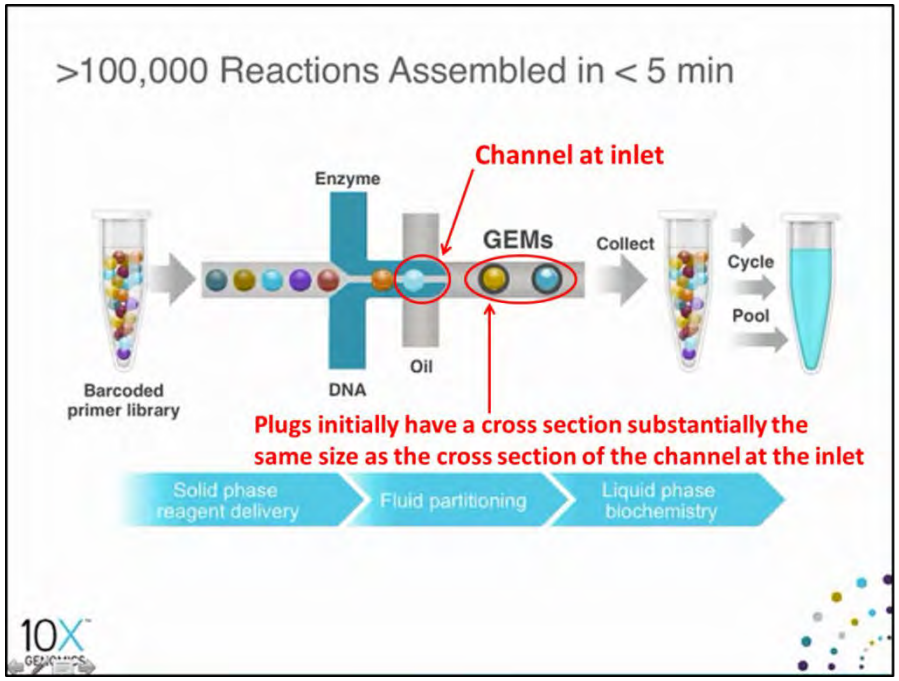
	’091 Claim Language	Infringement Support

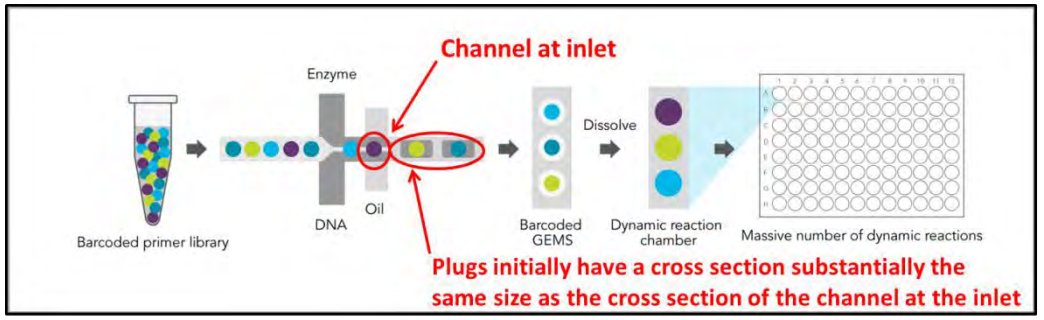


Id. at 1.

- 10x Technologies’ JP Morgan presentation further shows the plugs emerging from the junction of the oil (shown in gray) and the aqueous fluid containing the reagents (shown in blue):



	’091 Claim Language	Infringement Support
		Ex. 37 [JP Morgan presentation] at 2.
091-58	58. The method of claim 57, wherein each plug initially has a cross section that is substantially the same size as the cross section of the channel at the junction area.	**<u>The microfluidic droplets in 10X’s GemCode platform initially have a cross section that is substantially the same size as the cross section of the channel containing the aqueous fluids.</u>** • During his August webinar, Dr. Schnall-Levin explained that the picture below is “a cross-section of one of the ***channel in our microfluidic chip***.” *Id.* at 9:33-39. In that picture, each plug labeled GEMs has a cross section substantially the same size as the cross section as the cross section of the center channel. 

	'091 Claim Language	**Infringement Support**
		• 10x's website is also consistent in showing that the cross section of the plug is initially substantially the same size as the cross section of the center channel.  • 10x Technologies' 2015 presentation at the JP Morgan healthcare conference further shows a microfluidic system for conducting reactions in plugs, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are the light gray circles and initially have a cross section that is substantially the same as the cross section of the center channel.

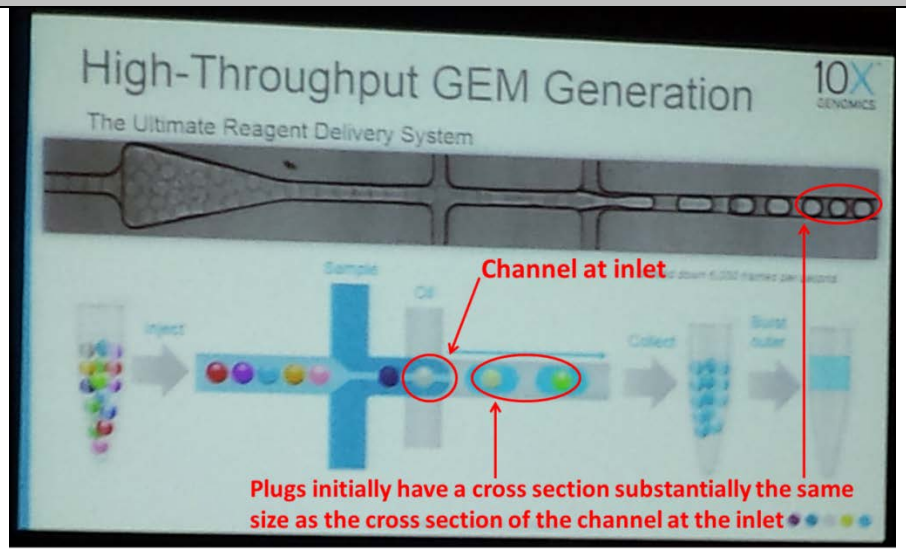
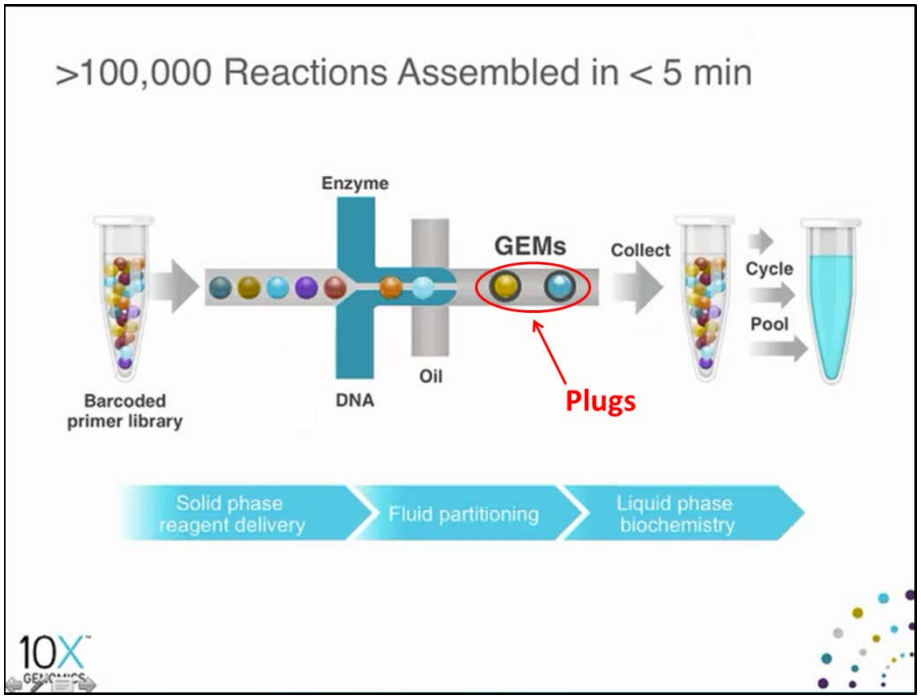
	’091 Claim Language	Infringement Support
		 Ex. 37 [JP Morgan presentation] at 2.

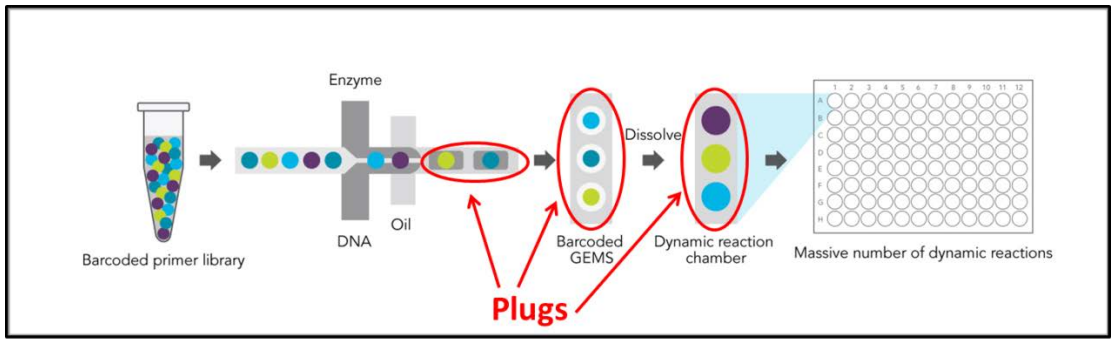
EXHIBIT 18

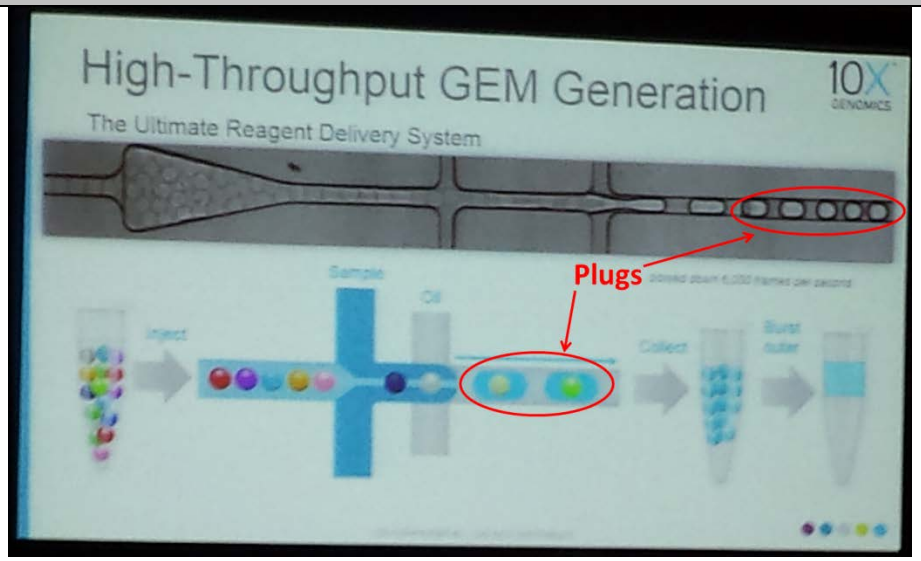
Infringement of U.S. Patent No. 8,304,193 by 10X's GemCode Platform[1]

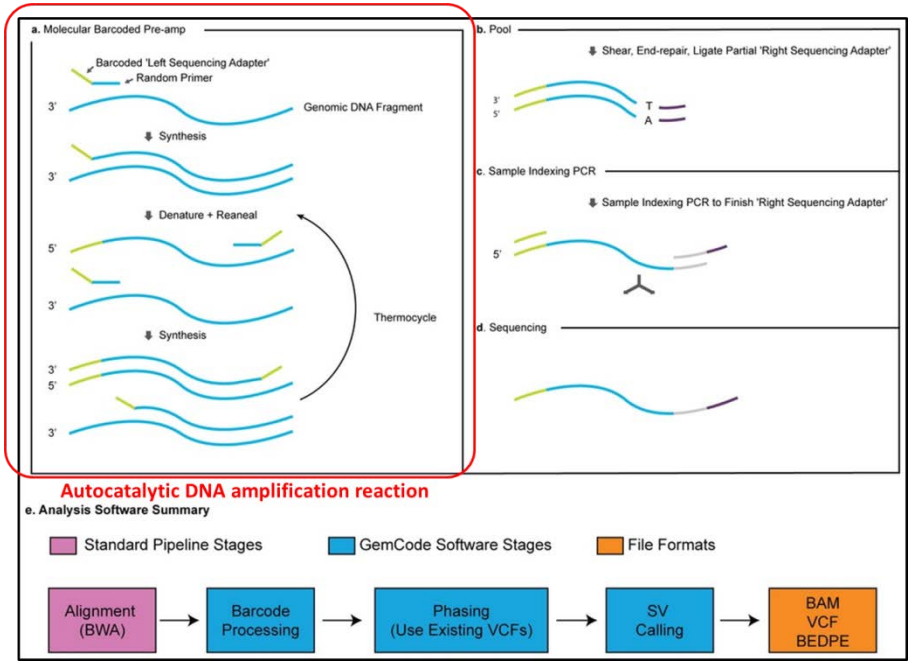
	'193 Claim Language	**Infringement Support**
193-1a	1. A method for conducting an autocatalytic reaction in plugs in a microfluidic system, comprising the steps of:	10X's GemCode platform uses "a method for conducting an autocatalytic reaction in plugs in a microfluidic system." • The microfluidic system is 10X's GemCode Instrument or Chromium Controller instrument. • The "plugs" are the microfluidic droplets that are formed in 10X's GemCode Instrument or Chromium Controller instrument. • The autocatalytic reaction is the DNA amplification reaction that is carried out in the droplets. **10X's GemCode Platform is a microfluidic system using "plugs," which 10X refers to as "droplets" or "GEMs"** • The '193 patent's description of "plugs" includes the following: "'Plugs' in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible." Ex. 12 ['193 patent] at 9:27-30. • On August 5, 2015, Michael Schnall-Levin, 10X's Vice President of Computational Biology and Applications, presented a webinar "about the GemCode platform." Ex. 4 [10X Webinar] at 3:17-3:23; *see also id.* at 3:35-38 ("I'm really excited today to take you through our Platform."). During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms plugs in the manner described by the '193 patent with reference to the below figure: "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in

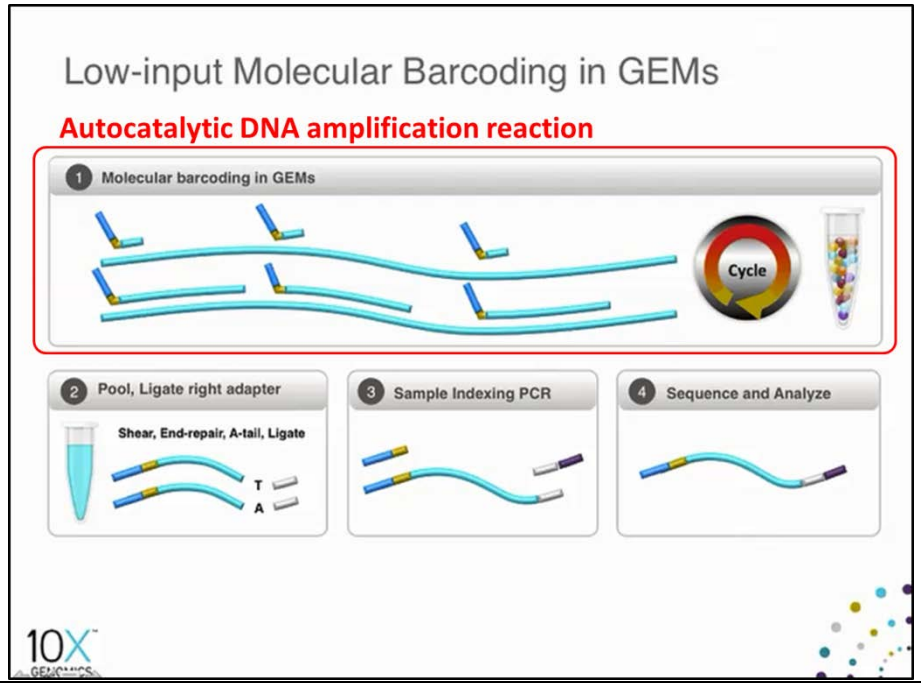
[1] The figures in this chart have been modified to include red annotations that more clearly identify the individual claim elements.

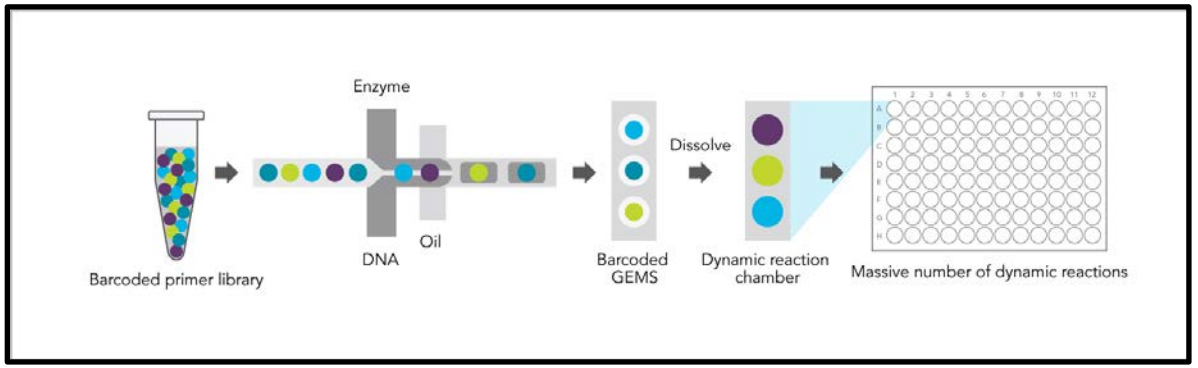
	’193 Claim Language	Infringement Support
		the oil provided again by 10X. There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***.” Ex. 4 [10X Webinar] at 9:48-10:39.  • 10x’s website is consistent with Dr. Schnall-Levin’s description of 10X’s Platform. 10X’s website states that “[t]he instrument features precise ***microfluidics*** coupled with single button, user-friendly operation.” Ex. 39 [10X Website Excerpts] at 3. The website further states that the 10X chip kit “[c]ontains the ***microfluidic chips*** and accessories required for sample partitioning.” *Id.* at 5.

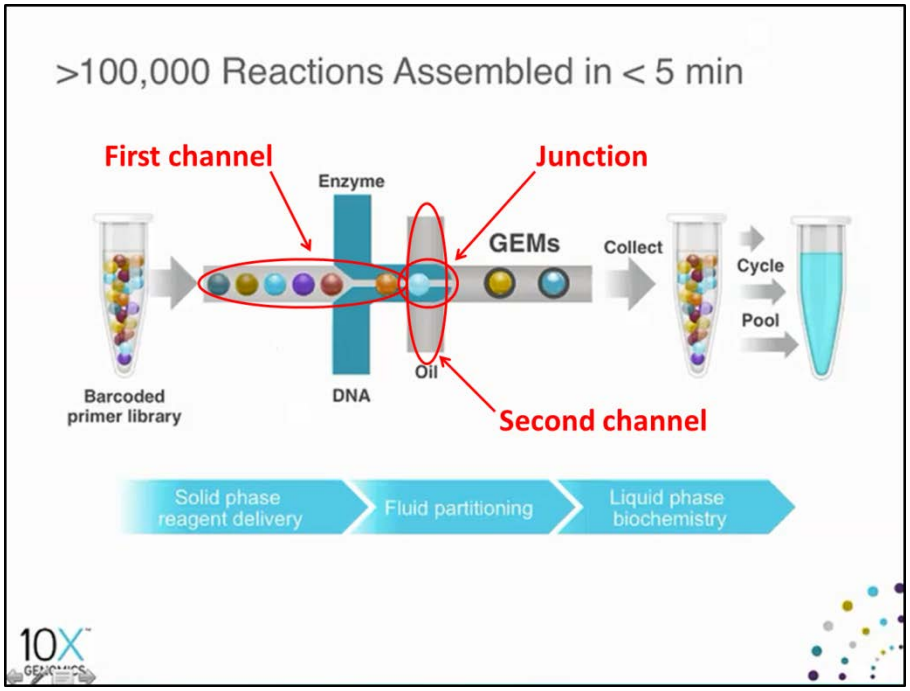
	’193 Claim Language	Infringement Support
		 *Id.* at 1. • 10x Technologies’ 2015 presentation at the JP Morgan healthcare conference further shows a microfluidic system for conducting reactions in plugs, including not just a schematic, but a micrograph of the actual microfluidic device. In the micrograph, the plugs are the light gray circles in the right most channel.

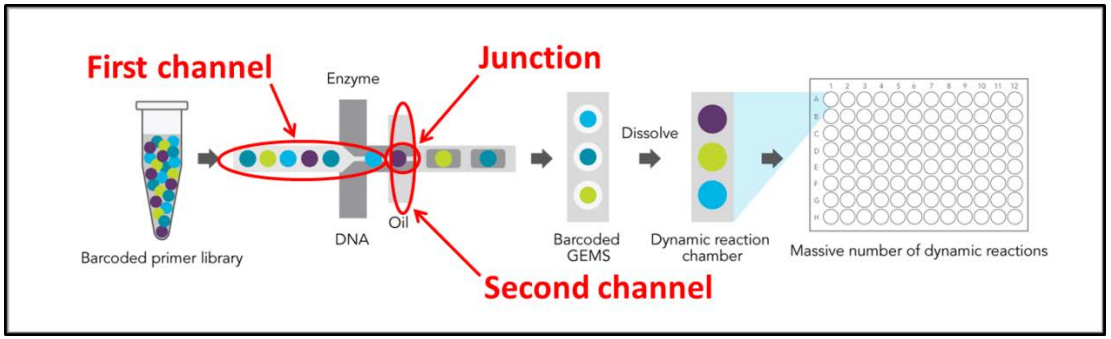
	’193 Claim Language	Infringement Support
		 Ex. 37 [JP Morgan Presentation] at 2. **10X’s GemCode platform conducts autocatalytic DNA amplification reactions within the microfluidic droplets (“plugs”)** • The slide above from 10X’s August 2015 presentation is entitled “>100,000 ***Reactions*** Assembled in <5 min,” which demonstrates that reactions are occurring within the microfluidic droplets. • The DNA amplification reaction that takes place in 10X’s product is an autocatalytic reaction. An autocatalytic reaction is a reaction in which the product of the reaction is also a reactant for the same reaction. The autocatalytic DNA amplification which take place within the microfluidic droplets is depicted in the figure below in the panel labeled “a. Molecular Barcoded Pre-amp,” which is taken from 10X’s recent article in *Nature*

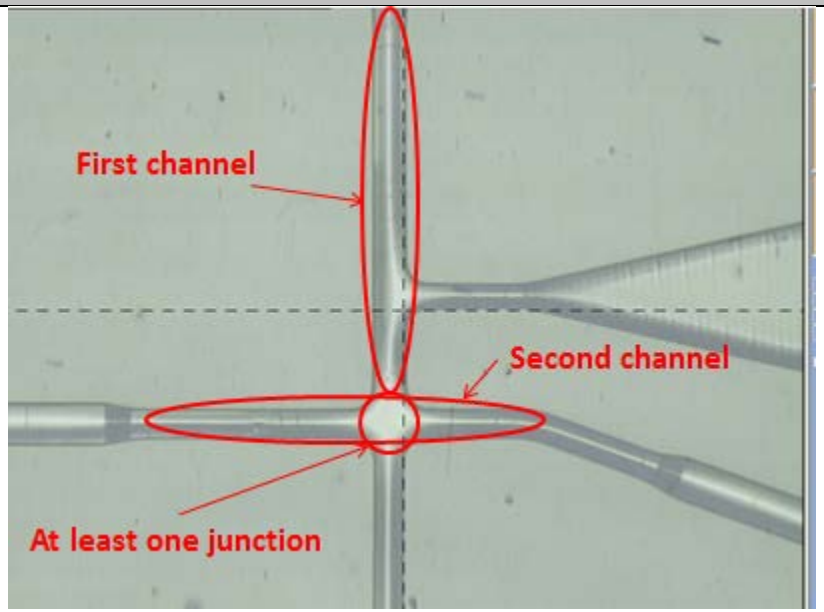
	’193 Claim Language	Infringement Support
		Biotechnology that presents data based on the use of 10X’s platform. The figure below shows a single stranded “Genomic DNA Fragment” that is extended through the use of a “Random Primer.” The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process. As the panel shows, the product of the first synthesis reaction is used as a reactant for another round of DNA synthesis. Hence, the reaction is autocatalytic.  Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X’s publication states, “1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes.” *Id.* at 3432. • During his August 2015 webinar, Dr. Schall-Levin also described the autocatalytic DNA

	’193 Claim Language	Infringement Support
		amplification reaction that takes place in the droplets with reference to the figure below. “So now the biochemistry that’s happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you’ve broken the droplets and put everything back together in bulk. First you can concentrate on the top panel showing the biochemistry that’s happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying.*** The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template.” Ex. 4 [10X Webinar] at 13:00-53. 

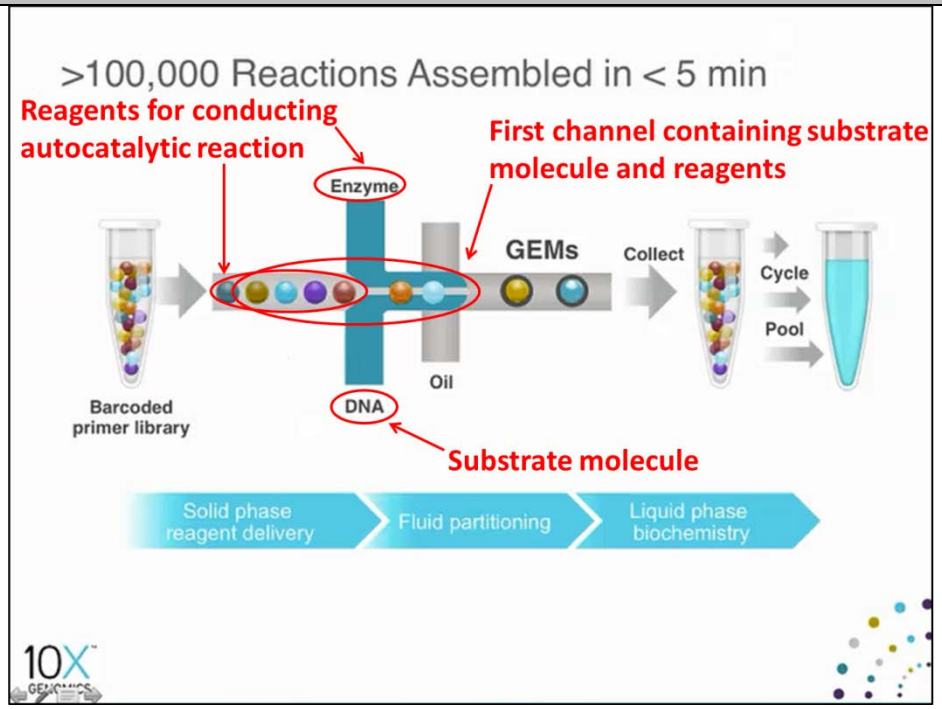
	'193 Claim Language	**Infringement Support**
		• The figure below from 10x's website depicts the microfluidic system wherein plugs are received in a "dynamic reaction chamber" wherein a "massive number of dynamic reactions" occur.  Ex. 37 [10X Website Excerpts] at 1.
193-1b	providing the microfluidic system comprising at least two channels having at least one junction;	10X's GemCode platform provides "the microfluidic system comprising at least two channels having at least one junction." • The first channel is the central channel where (1) the aqueous fluid containing the target DNA, (2) the aqueous fluid containing the enzyme and other reagents, and (3) the aqueous fluid containing the gel beads combine. • The second channel is the channel through which the oil is introduced. • The junction is where the central channel and the oil channel intersect. **10X's GemCode platform uses a microfluidic chip with at least a first channel that intersects a second channel.** • During his August webinar, Dr. Schnall-Levin explained that the picture below is "a cross-

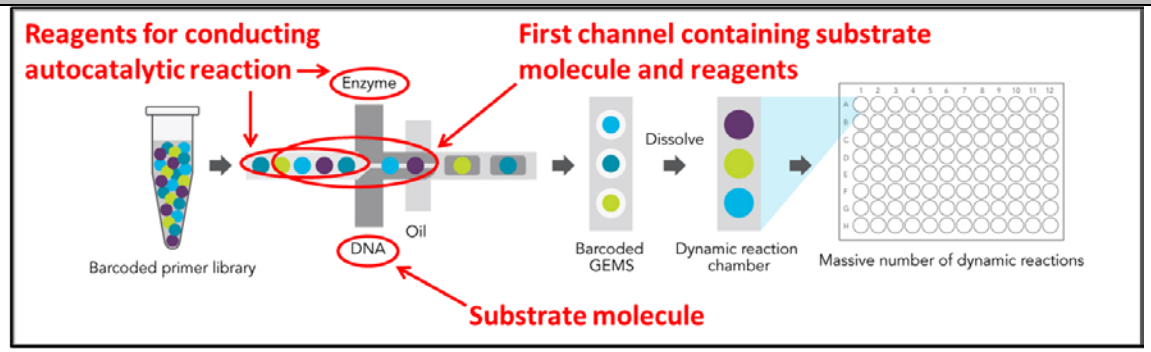
	’193 Claim Language	Infringement Support
		section of one of the ***channel in our microfluidic chip***.” *Id.* at 9:33-39. “If you look starting from left to right what you see is the channels that are from ***three different input wells***. On the ***first input well*** the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the ***second input well*** the user mixes our biochemical reagents with their DNA. And on the ***third input well*** the user puts in the oil provided again by 10X. ***There’s a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. They then flow through a second cross of oil*** which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead” *Id.* at 9:48-10:39. 

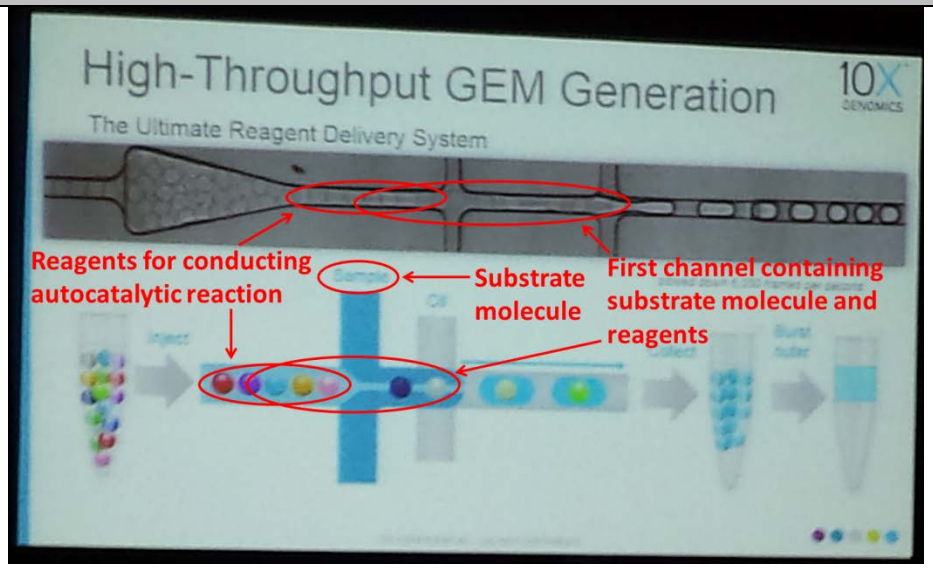
	'193 Claim Language	**Infringement Support**
		• 10x's website is consistent with Dr. Schnall-Levin's description of 10X's Platform. 10X's website states that "[t]he instrument features precise ***microfluidics*** coupled with single button, user-friendly operation." Ex. 39 [10X Website Excerpts] at 3. The website further states that the 10X chip kit "[c]ontains the ***microfluidic chips*** and accessories required for sample partitioning." *Id.* at 5. The figure below from 10x's website depicts the microfluidic system with at least two channels having at least one junction.  *Id.* at 1. • 10X's GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X's product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same inlet. This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below.

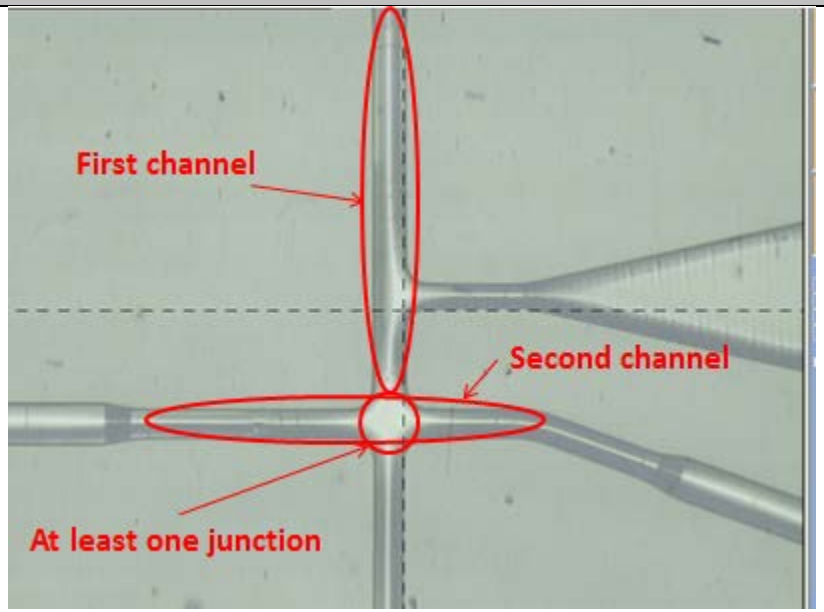
	'193 Claim Language	**Infringement Support**
		
193-1c	flowing an aqueous fluid containing at least one substrate molecule and reagents for conducting an autocatalytic reaction through a first channel of the at least two channels;	10X's GemCode platform "flow[s] an aqueous fluid containing at least one substrate molecule and reagents for conducting an autocatalytic reaction through a first channel of the at least two channels." • The aqueous fluid containing at least one substrate molecule and reagents for conducting an autocatalytic reaction is the combination of (1) the aqueous fluid that contains the user's sample DNA, (2) the aqueous fluid that contains 10X's barcoded gel beads, and (3) the aqueous fluid that contains enzymes and reagents that react with the DNA. • These three fluids combine at a first junction to yield a combined fluid that has substrate DNA and reagents, including at least primers and nucleotides. The primers are delivered via the gel beads. • The autocatalytic reaction that takes place is the amplification of DNA in the droplets. • The first channel is the central channel that perpendicularly intersects the oil channel.

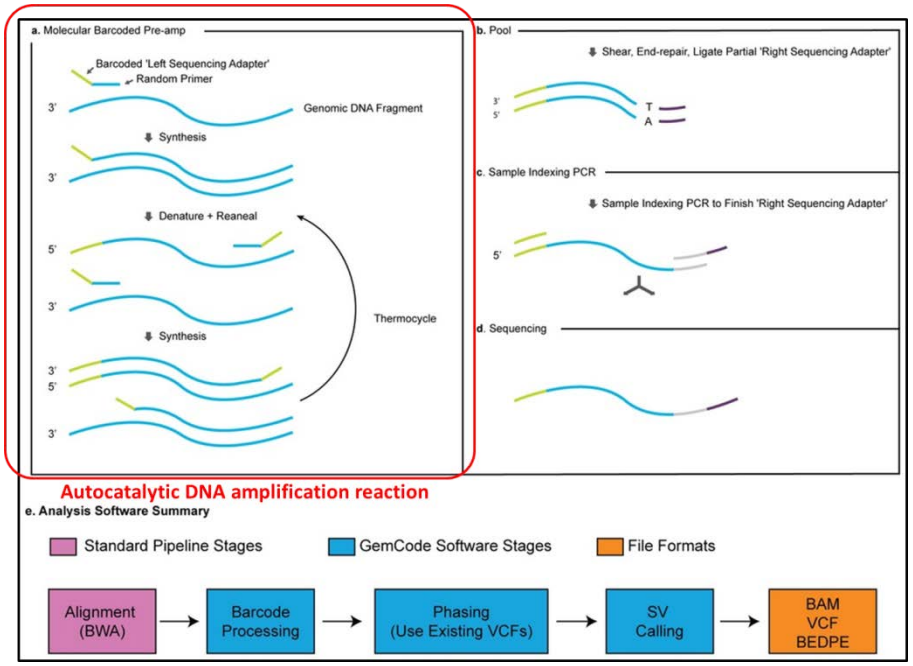
	'193 Claim Language	**Infringement Support**
		<u>10X's GemCode platform uses an aqueous fluid containing at least one substrate molecule (DNA) and at least one biochemical reagent (nucleotides and primers) that flows through a first channel of the microfluidic chip</u> • The '193 patent states that "Suitable reactants for use in the invention include synthetic small molecules, biological molecules (i.e., proteins, DNA, RNA, carbohydrates, sugars, etc.), metals and metal ions, and the like." Ex. 12 ['193 patent] at 20:10-13. Thus, in the '193 patent, "DNA" is a type of "substrate molecule." • During his August 5, 2015 presentation, Dr. Schnall-Levin explained that the picture below is "a cross-section of one of the channels in our microfluidic chip." Ex. 4 [10X Webinar] at 9:33-39. "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10x. ***On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly***. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead."*** *Id.* at 9:48-10:39. Thus, the aqueous solution of the gel beads, biochemical reagents and DNA ("substrate molecule") flow through a first channel.

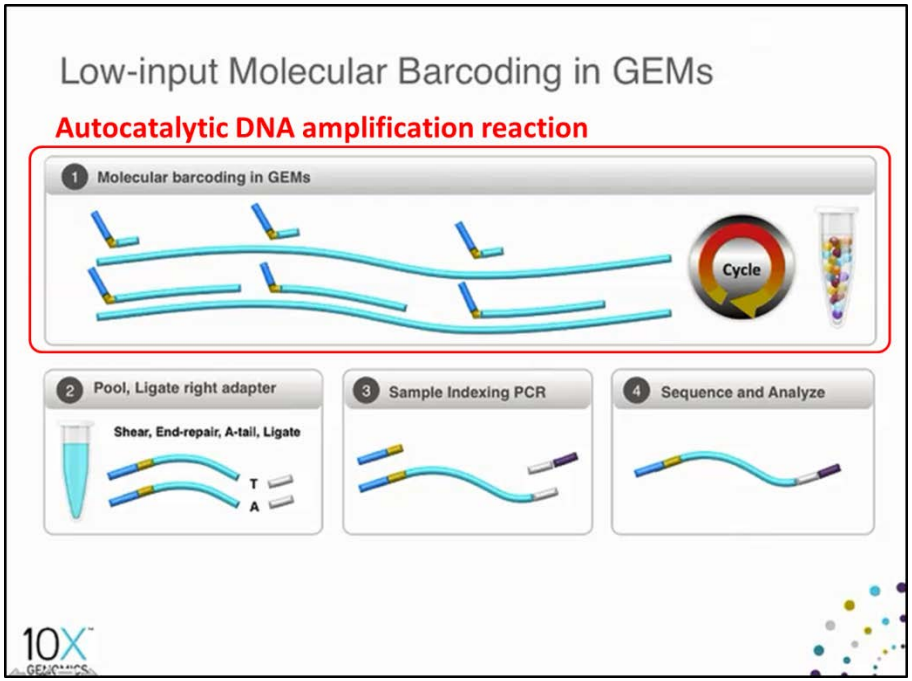
	’193 Claim Language	Infringement Support
		 • In the figure above, the aqueous solutions of DNA and enzyme are shown in blue flowing through a first channel. • The figure below from 10x’s website further notes the introduction of DNA for sequencing and enzyme through a continuously flowing aqueous solution through a central channel. It further shows a reaction taking place in a “Dynamic reaction chamber.”

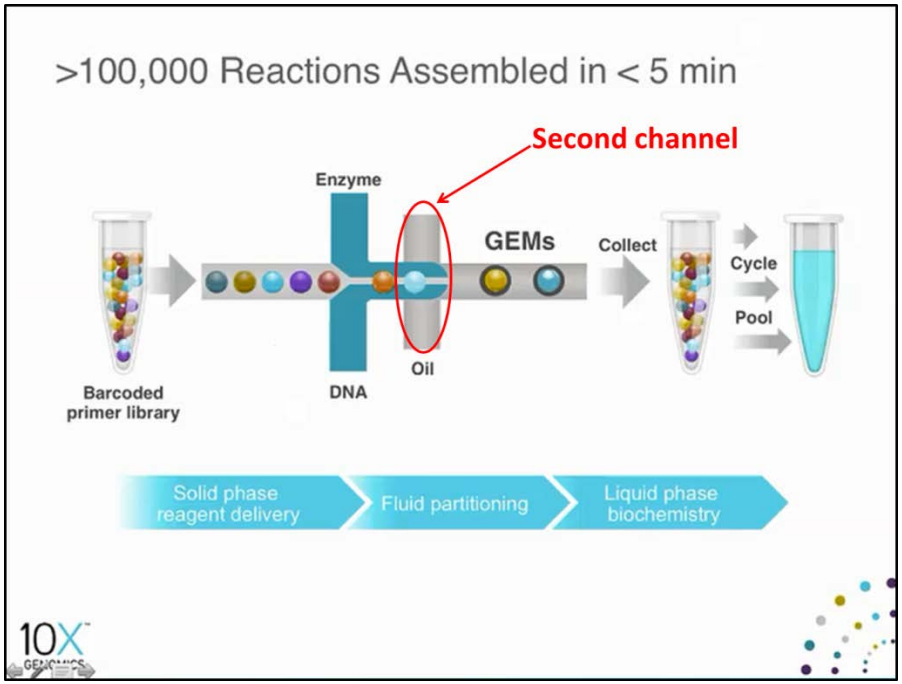
	’193 Claim Language	Infringement Support
		 Ex. 39 [10X Website Excerpts] at 1. • Similarly, 10X’s 2015 JP Morgan presentation shows a microfluidic system through which an aqueous fluid (shown in blue) flows and that contains a molecule (labeled as “sample”) and at least one other reagent (e.g., nucleotides) for subsequent use in a DNA amplification reaction.

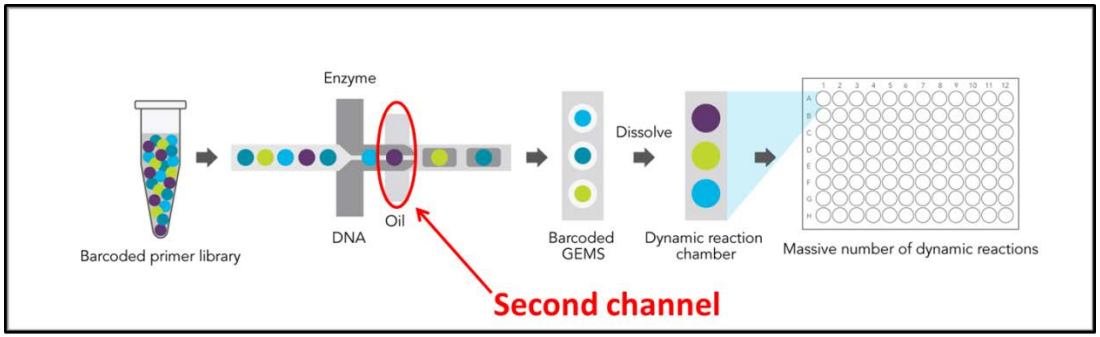
	'193 Claim Language	**Infringement Support**
		 Ex. 37 [JP Morgan Presentation] at 2. • 10X's GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X's product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same inlet. This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. The aqueous fluid containing the sample DNA ("substrate molecule") and enzyme/reagents flow through the channel labeled "first channel."

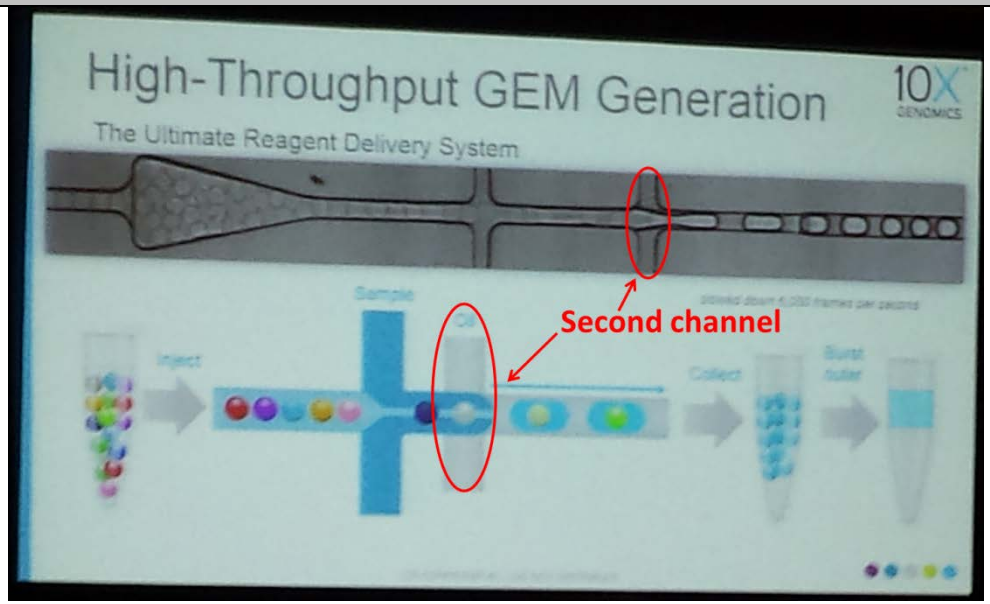
	'193 Claim Language	**Infringement Support**
		 **<u>The at least one biochemical reagent (nucleotides and primers) in the aqueous fluid is for conducting an autocatalytic reaction with the substrate molecule (DNA).</u>** • The DNA amplification reaction that takes place in 10X's GemCode platform is an autocatalytic reaction. An autocatalytic reaction is a reaction in which the product of the reaction is also a reactant for the same reaction. The autocatalytic DNA amplification which take place within the microfluidic droplets is depicted in the figure below in the panel labeled "a. Molecular Barcoded Pre-amp," which is taken from 10X's recent article in *Nature Biotechnology* that presents data based on the use of 10X's platform. The figure below shows a single stranded "Genomic DNA Fragment" that is extended through the use of a "Random Primer." The resulting double-stranded DNA fragment is then denatured, and the process is repeated through the thermocycling process. As the panel shows, the product of the first synthesis reaction is used as a reactant for another round of DNA synthesis.

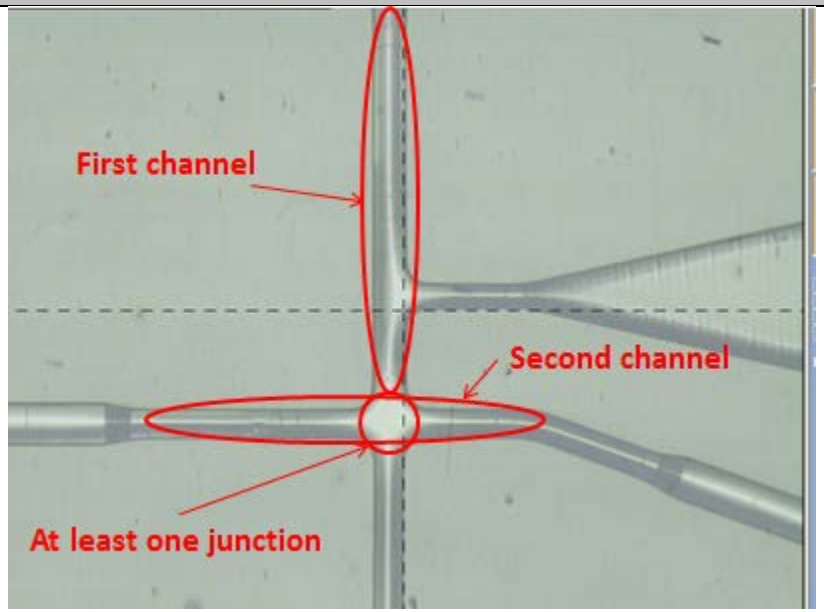
	’193 Claim Language	Infringement Support
		Hence, the reaction is autocatalytic. To carry out this reaction, the droplets include at least primers and nucleotides as reagents.  Ex. 5 [*Nature Biotechnology*] at Supp. Fig. 1. As 10X’s publication states, “1 ng of sample DNA was used for GEM reactions where DNA molecules were partitioned into droplets to ***amplify the DNA*** and introduce 14-bp partition barcodes.” *Id.* at 3432. • During his August 2015 webinar, Dr. Schall-Levin also described the autocatalytic DNA amplification reaction that takes place in the droplets with reference to the figure below. “So now the biochemistry that’s happening as part of the process. The biochemistry is divided into two major stages. The first happens inside of the droplets and the second happens after you’ve broken the droplets and put everything back together in bulk. First you

	’193 Claim Language	Infringement Support
		can concentrate on the top panel showing the biochemistry that’s happening inside the droplets. The droplets after coming off the instrument are placed in a standard 96-well plate and put on a thermal cycler for a thermal cycling protocol. ***During this thermal cycling protocol, oligos which have been released as the gel bead fall apart prime off of the genome and do a low-level of copying.*** The result is that you form molecules which contain one-half of the Illumina sequencing machinery containing the 10X barcode and a copy of the genomic template.” Ex. 4 [10X Webinar] at 13:00-53. 
193-1d	flowing an oil through the second channel of the at least	10X’s GemCode platform “flow[s] an oil through the second channel of the at least two channels.” • The second channel is the oil channel that perpendicularly intersects the central channel.

	'193 Claim Language	**Infringement Support**
	two channels;	**10X's GemCode platform continuously flows an oil through a second channel that intersects at a cross with a first channel containing an aqueous fluid.** • Dr. Schnall-Levin explained that in the below picture, "***on the third input well the user puts in the oil provided again by 10X***. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead"*** Id. at 9:48-10:39. Thus, the channel containing the oil intersects and flows into the channel containing the aqueous solution of the gel beads, biochemical reagents and DNA. 

	'193 Claim Language	**Infringement Support**
		• In the figure above the channel containing the continuously flowing oil is shown in grey. • The figure below from 10x's website further notes the continuously flowing oil from a second channel shown in light grey.  Ex. 39 [10X Website Excerpts] at 1. • Similarly, 10X's 2015 JP Morgan presentation shows a microfluidic system through which an aqueous fluid (shown in blue) flows and that contains a molecule (labeled as "sample") and at least one other reagent (e.g., nucleotides) for subsequent use in a DNA amplification reaction. The oil is shown in a second channel in light grey:

	’193 Claim Language	Infringement Support
		 Ex. 37 [JP Morgan Presentation] at 2. • 10X’s GemCode platform comprises eight microfluidic systems arranged in parallel. Below is a recent image of one such microfluidic system from 10X’s product. The geometry of the microfluidic system shown in this image is a variation of the arrangement depicted in the other figures in this chart. This arrangement functions in the same manner as the other arrangements depicted in this chart, except that the enzyme/reagents and sample DNA are delivered via the same inlet. This alternate arrangement of microfluidic channels still meets all elements of the claims, as shown in the annotated image below. The oil flows through the channel labeled “second channel.”

	'193 Claim Language	**Infringement Support**
		
193-1e	forming at least one plug of the aqueous fluid containing the at least one substrate molecule and reagents by partitioning the aqueous fluid with the flowing oil at the junction of the at least two channels, the plug being substantially surrounded by an oil	10X's GemCode platform forms "at least one plug of the aqueous fluid containing the at least one substrate molecule and reagents by partitioning the aqueous fluid with the flowing oil at the junction of the at least two channels, the plug being substantially surrounded by an oil flowing through the channel, wherein the at least one plug comprises at least one substrate molecule and reagents for conducting an autocatalytic reaction with the at least one substrate molecule." • The "plugs" are the microfluidic droplets that are formed at the junction between the oil and the aqueous fluid containing the substrate molecule and reagents. • The substrate molecule is the user's sample DNA • The reagents are nucleotides and primers (which are delivered via the gel beads) that are used in an autocatalytic DNA amplification reaction with the substrate DNA. **10X's GemCode platform forms microfluidic droplets ("plugs") by partitioning an aqueous**

	'193 Claim Language	**Infringement Support**
	flowing through the channel, wherein the at least one plug comprises at least one substrate molecule and reagents for conducting an autocatalytic reaction with the at least one substrate molecule; and	**<u>fluid flowing through a first channel with an oil flowing through a second channel such that the plugs are substantially surrounded by the oil.</u>** • The '193 patent's description of "plugs" includes the following: "'Plugs' in accordance with the present invention are formed in a substrate when a stream of at least one plug-fluid is introduced into the flow of a carrier-fluid in which it is substantially immiscible." Ex. 12 ['193 patent] at 9:27-30. • During his August 2015 presentation, Dr. Schnall-Levin described how 10X's microfluidic device forms plugs in the same manner as the '193 patent. The process is depicted in the figure below. "If you look starting from left to right what you see is the channels that are from three different input wells. On the first input well the user puts in the barcoded gel beads. This is a reagent delivered by 10X. On the second input well the user mixes our biochemical reagents with their DNA. And on the third input well the user puts in the oil provided again by 10X. There's a flow from left to right and the gel beads first flow through the mix of biochemical reagents and DNA mixing with them uniformly. ***They then flow through a second cross of oil which pinches off droplets each of which contain a small portion of the DNA from the user and a gel bead***." Ex. 4 [10X Webinar] at 9:48-10:39.